Barb O'Bryen

65913

Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: My-Chau Tran Examiner #: 78933 Date: 5/3/02
Art Unit: 1641 Phone Number 305-6999 Serial Number: ~~09/833,030~~ 09/849,924
Mail Box and Bldg/Room Location: ~~7E12~~ CM1, 8A16 Results Format Preferred (circle): (PAPER) DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need. 09-849924

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Affinity selected signature peptides for protein identification and quantification.

Inventors (please provide full names): Fred E. Regnier, Xiang Zhang, and Asish Chakraborty

Earliest Priority Filing Date: 5/5/2000

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Mrs. O'Bryen,

I'm search for a method of analyzing proteins and/or peptides by mass spectroscopy of interest. The mass. spectroscopy of interest are: 1) MALDI (matrix assisted laser desorption ionization, 2) ESI (electrospray ionization) and 3) APCI (atmospheric pressure chemical ionization. Please perform ~~or~~ ~~enclosed~~

1) Inventors search
2) search of independent claim 6, 33 + 34 (enclosed).

Also attached is the abstract as an aid.

Thank-you.

Point of Contact:
Barb O'Bryen
Technical Information Specialist
STIC CM1 6A05 308-4291

****

STAFF USE ONLY BOB **Type of Search** **Vendors and cost where applicable**

Searcher Phone #: _____	AA Sequence (#) _____	Dialog _____
Searcher Location: _____	Structure (#) _____	Questel/Orbit _____
Date Searcher Picked Up: _____	Bibliographic 0	Dr.Link _____
Date Completed: 5-10-02	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: _____	Fulltext _____	Sequence Systems _____
Clerical Prep Time: _____	Patent Family _____	WWW/Internet _____
Online Time: _____	Other _____	Other (specify) _____

PTO-1590 (8-01)

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=> fil hcapl; d que 14
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Inventor search

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FILE COVERS 1907 - 10 May 2002  VOL 136 ISS 19
FILE LAST UPDATED: 8 May 2002  (20020508/ED)

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L1  (       336)SEA FILE=CAPLUS ABB=ON  REGNIER F?/AU
L2  (     18226)SEA FILE=CAPLUS ABB=ON  ZHANG X?/AU
L3  (       584)SEA FILE=CAPLUS ABB=ON  CHAKRABORTY A?/AU
L4            3 SEA FILE=HCAPLUS ABB=ON  L1 AND L2 AND L3


=> fil wpids; d que 18; d que 113; s l8 or l13

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FILE LAST UPDATED: 08 MAY 2002              <20020508/UP>
MOST RECENT DERWENT UPDATE           200229  <200229/DW>
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>>> The BATCH option for structure searches has been
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L5  (        29)SEA FILE=WPIDS ABB=ON  REGNIER F?/AU
L6  (      1628)SEA FILE=WPIDS ABB=ON  ZHANG X?/AU
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Searched by Barb O'Bryen, STIC 308-4291

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L7  (        22)SEA FILE=WPIDS ABB=ON  CHAKRABORTY A?/AU
L8            1 SEA FILE=WPIDS ABB=ON  L5 AND L6 AND L7


L9  (        29)SEA FILE=WPIDS ABB=ON  REGNIER F?/AU
L10 (      1628)SEA FILE=WPIDS ABB=ON  ZHANG X?/AU
L11 (        22)SEA FILE=WPIDS ABB=ON  CHAKRABORTY A?/AU
L12 (      6505)SEA FILE=WPIDS ABB=ON  MASS SPECTR?
L13           2 SEA FILE=WPIDS ABB=ON  L12 AND ((L9 OR L10 OR L11))


L156          2 L8 OR L13

=> fil medl; d que l17; d que l23; s l17 or l23

FILE 'MEDLINE' ENTERED AT 12:53:54 ON 10 MAY 2002

 FILE LAST UPDATED: 9 MAY 2002 (20020509/UP).  FILE COVERS 1958 TO DATE.

 On April 22, 2001, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE now contains IN-PROCESS records.  See HELP CONTENT for details.

 MEDLINE is now updated 4 times per week.  A new current-awareness alert
 frequency (EVERYUPDATE) is available.  See HELP UPDATE for more information.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2001 vocabulary.  Enter HELP THESAURUS for details.

 The OLDMEDLINE file segment now contains data from 1958 through 1965.
 Enter HELP CONTENT for details.

 Left, right, and simultaneous left and right truncation are available in the
 Basic Index.  See HELP SFIELDS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
 SUBSTANCE IDENTIFICATION.


L14 (       180)SEA FILE=MEDLINE ABB=ON  REGNIER F?/AU
L15 (      3824)SEA FILE=MEDLINE ABB=ON  ZHANG X?/AU
L16 (       278)SEA FILE=MEDLINE ABB=ON  CHAKRABORTY A?/AU
L17           1 SEA FILE=MEDLINE ABB=ON  L14 AND L15 AND L16


L18 (       180)SEA FILE=MEDLINE ABB=ON  REGNIER F?/AU
L19 (      3824)SEA FILE=MEDLINE ABB=ON  ZHANG X?/AU
L20 (       278)SEA FILE=MEDLINE ABB=ON  CHAKRABORTY A?/AU
L21 (     50264)SEA FILE=MEDLINE ABB=ON  SPECTRUM ANALYSIS, MASS+NT/CT
L22 (         5)SEA FILE=MEDLINE ABB=ON  (L18 AND (L19 OR L20)) OR (L19 AND
                 L20)
L23           2 SEA FILE=MEDLINE ABB=ON  L21 AND L22


L157          2 L17 OR L23

=> fil embase; d que l27;d que l34; s l27 or l34

FILE 'EMBASE' ENTERED AT 12:53:55 ON 10 MAY 2002
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FILE COVERS 1974 TO 8 May 2002 (20020508/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L24 (       139)SEA FILE=EMBASE ABB=ON  REGNIER F?/AU
L25 (      3095)SEA FILE=EMBASE ABB=ON  ZHANG X?/AU
L26 (       213)SEA FILE=EMBASE ABB=ON  CHAKRABORTY A?/AU
L27           1 SEA FILE=EMBASE ABB=ON  L24 AND L25 AND L26


L28 (       139)SEA FILE=EMBASE ABB=ON  REGNIER F?/AU
L29 (      3095)SEA FILE=EMBASE ABB=ON  ZHANG X?/AU
L30 (       213)SEA FILE=EMBASE ABB=ON  CHAKRABORTY A?/AU
L31 (     58444)SEA FILE=EMBASE ABB=ON  MASS SPECTROMETRY+NT/CT
L32 (     43091)SEA FILE=EMBASE ABB=ON  PROTEIN ANALYSIS/CT
L33 (     17638)SEA FILE=EMBASE ABB=ON  L32/MAJ
L34           4 SEA FILE=EMBASE ABB=ON  (L28 OR L29 OR L30) AND L31 AND L33


L158          4 L27 OR L34

=> fil jic biosis biotechno anabstr

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=> d que l129;d que l137; s l129 or l137

L121         401 SEA REGNIER F?/AU
L122        8796 SEA ZHANG X?/AU
L123         466 SEA CHAKRABORTY A?/AU
L129           4 SEA L121 AND L122 AND L123


L121         401 SEA REGNIER F?/AU
L122        8796 SEA ZHANG X?/AU
L123         466 SEA CHAKRABORTY A?/AU
L126          30 SEA SIGNATURE#(2A) PEPTIDE#
L127      140112 SEA MASS SPECTR?
L137          11 SEA L126 AND ((L121 OR L122 OR L123)) AND L127


L159         11 L129 OR L137
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=> dup rem l157,l4,l159,l158,l156
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PROCESSING COMPLETED FOR L4
PROCESSING COMPLETED FOR L159
PROCESSING COMPLETED FOR L158
PROCESSING COMPLETED FOR L156
L160          11 DUP REM L157 L4 L159 L158 L156 (11 DUPLICATES REMOVED)
                 ANSWERS '1-2' FROM FILE MEDLINE
                 ANSWERS '3-4' FROM FILE HCAPLUS
                 ANSWERS '5-8' FROM FILE BIOSIS
                 ANSWERS '9-10' FROM FILE EMBASE
                 ANSWER '11' FROM FILE WPIDS

=> d ibib ab 1-11

L160 ANSWER 1 OF 11     MEDLINE                          DUPLICATE 5
ACCESSION NUMBER:   2000445940     MEDLINE
DOCUMENT NUMBER:    20450521   PubMed ID: 10997715
TITLE:              Strategy for qualitative and quantitative analysis in
                    proteomics based on signature peptides.
AUTHOR:             Ji J; Chakraborty A; Geng M; Zhang X;
                    Amini A; Bina M; Regnier F
CORPORATE SOURCE:   Department of Chemistry, Purdue University, Lafayette, IN
                    47907, USA.
CONTRACT NUMBER:    GM 59996 (NIGMS)
SOURCE:             JOURNAL OF CHROMATOGRAPHY. B, BIOMEDICAL SCIENCES AND
                    APPLICATIONS, (2000 Aug 4) 745 (1) 197-210.
                    Journal code: CXN. ISSN: 1387-2273.
PUB. COUNTRY:       Netherlands
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200101
ENTRY DATE:         Entered STN: 20010322
                    Last Updated on STN: 20010322
                    Entered Medline: 20010111
AB   This paper describes a new analytical strategy for identifying proteins in
     concentration flux based on isotopic labeling peptides in tryptic digests.
     Primary amino groups in peptides from control and experimental samples
     were derivatized with acetate and trideuteroacetate, respectively. After
     mixing samples thus labeled from these two sources, the relative
     concentration of peptides was determined by isotope ratio analysis with
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MALDI and ESI mass spectrometry. More than a 100-fold difference in relative concentration could be detected. Simplification of complex tryptic digests prior to mass spectral analysis was achieved by selection of histidine-containing peptides with immobilized metal affinity sorbents or of glycopeptides by lectin columns. Because most of these peptides have sequences that are unique to a single protein, they are a signature of the protein from which they were derived; providing a facile route to protein analysis.

L160 ANSWER 2 OF 11 MEDLINE
ACCESSION NUMBER: 2001175513 MEDLINE
DOCUMENT NUMBER: 21169933 PubMed ID: 11270868
TITLE: Proteomics of glycoproteins based on affinity selection of glycopeptides from tryptic digests.
AUTHOR: Geng M; **Zhang X**; Bina M; **Regnier F**
CORPORATE SOURCE: Department of Chemistry, Purdue University, Lafayette, IN 47907-1393, USA.
CONTRACT NUMBER: GM-59996 (NIGMS)
SOURCE: JOURNAL OF CHROMATOGRAPHY. B, BIOMEDICAL SCIENCES AND APPLICATIONS, (2001 Mar 10) 752 (2) 293-306.
Journal code: CXN; 9714109. ISSN: 1387-2273.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010709
Last Updated on STN: 20010709
Entered Medline: 20010705

AB Identification of glycoproteins in complex mixtures derived from either human blood serum or a cancer cell line was achieved in a process involving the steps of (1) reduction and alkylation, (2) proteolysis of all proteins in the mixture with trypsin, (3) affinity chromatographic selection of the glycopeptides with an immobilized lectin, (4) direct transfer of the glycopeptide fraction to a reversed-phase liquid chromatography (RPLC) column and further fractionation by gradient elution, (5) matrix-assisted laser desorption ionization mass spectrometry of individual fractions collected from the RPLC column, and (6) peptide identification based on a database search. The types of glycoproteins analyzed were; (1) N-type glycoproteins of known primary structure, (2) N-type glycoproteins of unknown structure, and (3) O-type glycoproteins glycosylated with a single N-acetylglucosamine. Identification of peptides from complex mixtures was greatly facilitated by either C-terminal sequencing with a carboxypeptidase mixture or by comparing chromatographic behavior and mass to standards, as in the case of a known protein. In addition, deglycosylation of peptides with N glycosidase F was necessary to identify N-type glycoproteins of unknown structure. The strength of this approach is that it is fast and targets specific molecular species or classes of glycoproteins for identification. The weakness is that it does not discriminate between glycoforms.

L160 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 2001:833654 HCAPLUS
DOCUMENT NUMBER: 135:354995
TITLE: Affinity selected signature peptides for protein identification and quantification
INVENTOR(S): **Regnier, Fred E.**; **Chakraborty, Asish B.**; Dormady, Shelly J.; G'eng, Minghui; Ji, Junyan; Riggs, Larry D.; Sioma, Cathy S.; Wang, Shihong; **Zhang, Xiang**
PATENT ASSIGNEE(S): Purdue Research Foundation, USA
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2

Searched by Barb O'Bryen, STIC 308-4291

[redacted]

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001086306	A2	20011115	WO 2001-US14418	20010504
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002037532	A1	20020328	US 2001-849924	20010504

PRIORITY APPLN. INFO.: US 2000-203227P P 20000505
US 2000-208184P P 20000531
US 2000-208372P P 20000531

AB A method for protein identification in complex mixts. is described that utilizes affinity selection of constituent proteolytic peptide fragments unique to a protein analyte. These "signature peptides" function as anal. surrogates. Mass spectrometric anal. of the proteolyzed mixt. permits identification of a protein in a complex sample without purifying the protein or obtaining its composite peptide signature.

L160 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
ACCESSION NUMBER: 2001:142678 HCAPLUS
DOCUMENT NUMBER: 134:307375
TITLE: Multidimensional chromatography and the signature peptide approach to proteomics
AUTHOR(S): **Regnier, Fred**; Amini, Ahmad; **Chakraborty, Asish**; Geng, Ming; Ji, Junyan; Riggs, Larry; Sioma, Cathy; Wang, Shihong; **Zhang, Xiang**
CORPORATE SOURCE: Department of Chemistry, Purdue Univ., West Lafayette, IN, 47907, USA
SOURCE: LCGC North America (2001), 19(2), 200, 202, 204, 206, 208, 210, 212-213
CODEN: LNACBH; ISSN: 1527-5949
PUBLISHER: Advanstar Communications, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 41 refs. Advances in genomics during the past decade have drawn enormous attention to the ability to obtain greater amt. of information in as little time as possible. Although these advances represent great gains, they pale in comparison to the dynamic complexity of the next generation of study, proteomics. Until recently, gel electrophoresis and chem. sequencing have dominated proteomics, but the field of proteomics now has a new group of tools, which includes the identification and monitoring of up- and down-regulation of proteins. Affinity chromatog., mass spectrometry and bioinformatics allow users to qual. and quant. identify the thousands of potential signature peptides generated by a proteomics tryptic digest.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L160 ANSWER 5 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC. DUPLICATE 2
ACCESSION NUMBER: 2001:447319 BIOSIS
DOCUMENT NUMBER: PREV200100447319

TITLE: Automated **signature peptide** approach for proteomics.
AUTHOR(S): Riggs, Larry; Sioma, Cathy; **Regnier, Fred E. (1)**
CORPORATE SOURCE: (1) Department of Chemistry, Purdue University, West Lafayette, IN, 47907: fregnier@purdue.edu USA
SOURCE: Journal of Chromatography A, (27 July, 2001) Vol. 924, No. 1-2, pp. 359-368. print.
ISSN: 0021-9673.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB This paper addresses the issue of automating the multidimensional chromatographic, **signature peptide** approach to proteomics. Peptides were automatically reduced and alkylated in the autosampler of the instrument. Trypsin digestion of all proteins in the sample was then executed on an immobilized enzyme column and the digest directly transferred to an affinity chromatography column. Although a wide variety of affinity columns may be used, the specific column used in this case was a Ga(III) loaded immobilized metal affinity chromatography (IMAC) column. Ga(III)-IMAC is known to select phosphorylated peptides. Phosphorylated peptides selected by the affinity column from tryptic digests of milk were automatically transferred to a reversed-phase liquid chromatography (RPLC) column. Further fractionation of tryptic peptides on the RPLC column was achieved with linear solvent gradient elution. Effluent from the RPLC column was electrosprayed into a time-of-flight **mass spectrometer**. The entire process was controlled by software in the liquid chromatograph. With slight modification, it is possible to add multiple columns in parallel at any of the single column positions to further increase throughput. Total analysis time in the tandem column mode of operation was under 2 h.

L160 ANSWER 6 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
ACCESSION NUMBER: 2000:166163 BIOSIS
DOCUMENT NUMBER: PREV200000166163
TITLE: **Signature-peptide** approach to detecting proteins in complex mixtures.
AUTHOR(S): Geng, Minghui; Ji, Junyan; **Regnier, Fred E. (1)**
CORPORATE SOURCE: (1) Department of Chemistry, Purdue University, West Lafayette, IN, 47907 USA
SOURCE: Journal of Chromatography A., (Feb. 18, 2000) Vol. 870, No. 1-2, pp. 295-313.
ISSN: 0021-9673.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The objective of the work presented in this paper was to test the concept that tryptic peptides may be used as analytical surrogates of the protein from which they were derived. Proteins in complex mixtures were digested with trypsin and classes of peptide fragments selected by affinity chromatography, lectin columns were used in this case. Affinity selected peptide mixtures were directly transferred to a high-resolution reversed-phase chromatography column and further resolved into fractions that were collected and subjected to matrix-assisted laser desorption ionization (MALDI) **mass spectrometry**. The presence of specific proteins was determined by identification of **signature peptides** in the **mass spectra**. Data are also presented that suggest proteins may be quantified as their **signature peptides** by using isotopically labeled internal standards. Isotope ratios of peptides were determined by MALDI **mass spectrometry** and used to determine the concentration of a peptide relative to that of the labeled internal standard. Peptides in tryptic digests were labeled by acetylation with

acetyl N-hydroxysuccinimide while internal standard peptides were labeled with the trideuteroacetylated analogue. Advantages of this approach are that (i) it is easier to separate peptides than proteins, (ii) native structure of the protein does not have to be maintained during the analysis, (iii) structural variants do not interfere and (iv) putative proteins suggested from DNA databases can be recognized by using a **signature peptide** probe.

L160 ANSWER 7 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:284804 BIOSIS
DOCUMENT NUMBER: PREV200200284804
TITLE: Minimizing resolution of isotopically coded peptides in comparative proteomics.
AUTHOR(S): Zhang, Roujian; **Regnier, Fred E. (1)**
CORPORATE SOURCE: (1) Department of Chemistry, Purdue University, West Lafayette, IN, 47907: fregnier@purdue.edu USA
SOURCE: Journal of Proteome Research, (March April, 2002) Vol. 1, No. 2, pp. 139-147. http://pubs.acs.org/JPR. print. ISSN: 1535-3893.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Stable isotopes are now widely used to quantify concentration changes in proteomics. This paper focuses on the resolution of isotopically coded peptides and how isotope effects occurring during chromatographic separations can be minimized. Heavy isotope derivatizing agents used in this work were the commercially available 2H8-ICAT reagent and 13C4-succinic anhydride. The ICAT reagent derivatizes cysteine-containing peptides, whereas the succinic anhydride reacts with primary amine groups in peptides. It was observed during reversed-phase chromatography of peptides from a BSA tryptic digest differentially labeled with the 2H0- and 2H8-ICAT reagents that resolution of the isoforms exceeded 0.5 with 20% of the peptides in the digest. Three-fourths of the peptides in this group contained two cysteine residues and were doubly labeled. Only 23% of the peptides labeled with a single ICAT residue had a resolution greater than 0.4. The resolution of peptides differentially labeled with 13C- and 12C-succinate never exceeded +-0.01, even in the case of peptides from the BSA digest labeled with 2 mol of succinate. Because this value is within the limits of the method used to determine resolution, it was concluded the 13C- and 12C-coded isoforms of labeled peptides did not resolve. The isotope ratio in the case of 13C/12C coding could be determined from a single **mass spectrum** taken at any point in the elution profile. This enabled isotope ratio analysis to be completed early in the elution of a peptide from chromatography columns.

L160 ANSWER 8 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:438709 BIOSIS
DOCUMENT NUMBER: PREV200000438709
TITLE: Identification of up-regulated protein in E. coli based on **signature peptides** approach.
AUTHOR(S): **Chakraborty, Asish (1); Regnier, Fred E. (1)**
CORPORATE SOURCE: (1) Department of Chemistry, Purdue University, 1393 Brown Building, West Lafayette, IN, 47907 USA
SOURCE: Abstracts of Papers American Chemical Society, (2000) Vol. 220, No. Part 1, pp. ANYL 158. print. Meeting Info.: 220th National Meeting of the American Chemical Society Washington DC, Washington DC, USA August 20-24, 2000 American Chemical Society . ISSN: 0065-7727.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L160 ANSWER 9 OF 11 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002123616 EMBASE
TITLE: Proteomic analysis of differential protein expression in human nasopharyngeal carcinoma cells induced by NAG7 transfection.
AUTHOR: Tan C.; Li J.; Wang J.; Xiang Q.; **Zhang X.**; Dong L.; Shen S.; Liang S.; Li G.
CORPORATE SOURCE: Dr. G. Li, Cancer Research Institute, School of Xiangya Medicine, Central South University, No. 88, Xiangya Road, Changsha 410078, Hunan, China. ligy@public.cs.hn.cn
SOURCE: Proteomics, (2002) 2/3 (306-312).
Refs: 29
ISSN: 1615-9853 CODEN: PROTC7
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Nasopharyngeal carcinoma (NPC) is a commonly occurring tumor in southern China and south east Asia. A genetic factor has now been recognized to be associated with this cancer. A new gene, named NAG7, was cloned from the common minimal deletion region in 3p25.3-26.3. In order to investigate the function of NAG7 gene, proteomic methods were used to find and identify the differential proteins and expected to elucidate the mechanism of NAG7. The NAG7 eukaryotic expression vector was constructed and transfected into NPC cell line HNE1 with liposome. Twenty-two differential protein spots in transfected cells were found significant and reproducible using high-resolution two-dimensional electrophoresis. Nine proteins that were up-regulated and seven proteins that were down-regulated were identified by matrix assisted laser desorption/ionization time of flight mass spectrometry and database analysis. These proteins included growth arrest specific protein, DNA binding protein, caspase 6, pinch protein and ras-related protein rab-36, which are involved in cell cycling, transcription regulation, signaling pathways and apoptosis. NAG7 may exert its functions by mediating differential expression of these proteins.

L160 ANSWER 10 OF 11 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96328595 EMBASE
DOCUMENT NUMBER: 1996328595
TITLE: Characterization of unstable intermediates and oxidized products formed during cyanogen bromide cleavage of peptides and proteins by electrospray mass spectrometry.
AUTHOR: **Zhang X.**; Dillen L.; Vanhoutte K.; Van Dongen W.; Esmans E.; Claeys M.
CORPORATE SOURCE: Dept. of Pharmaceutical Sciences, University of Antwerp, Universiteitsplein 1,B-2610 Antwerp, Belgium
SOURCE: Analytical Chemistry, (1996) 68/19 (3422-3430).
ISSN: 0003-2700 CODEN: ANCHAM
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Products formed during cyanogen bromide (CNBr) digestion of .alpha.-endorphin, .beta.-endorphin, and horse heart myoglobin are examined using reversed-phase high-performance liquid chromatography and electrospray mass spectrometry. It is demonstrated that unstable intermediate reaction products may be formed, as well as oxidized products when the CNBr reaction is performed in 0.1% TFA in water/acetonitrile (6:4 v/v) and that, under other conditions commonly employed for the CNBr

cleavage reaction, unstable intermediate products are also generated. The formation of the expected cleavage product's is found to be improved by adjusting the hydrolysis conditions. The structure of the intermediate formed from .alpha.-endorphin is examined using electrospray mass spectrometry in combination with low-energy collision-induced dissociation and tandem mass spectrometry and is shown to have a cyclic hydrated homoserine iminolactone part. The results obtained in this study explain the formation of partially cleaved proteins in the case of Met-Thr-containing sequences, which likely have a cyclic hydrated homoserine iminolactone part instead of the putative homoserine residue.

L160 ANSWER 11 OF 11 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2001-061888 [07] WPIDS
DOC. NO. NON-CPI: N2001-046366
DOC. NO. CPI: C2001-017286
TITLE: Addition of electron to chemical deposited on surface useful for detecting analytes by laser desorption **mass spectrometry** comprises exposing surface to light to release electron from surface or from second chemical on surface.
DERWENT CLASS: B04 S03 V05
INVENTOR(S): GIESE, R W; WANG, P; **ZHANG, X**
PATENT ASSIGNEE(S): (UYNE-N) UNIV NORTHEASTERN
COUNTRY COUNT: 20
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000077812	A2	20001221	(200107)*	EN	36

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: JP US

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000077812	A2	WO 2000-US40173	20000608

PRIORITY APPLN. INFO: US 1999-139170P 19990615; US 1999-138466P 19990610

AB WO 200077812 A UPAB: 20011129
NOVELTY - A method of adding an electron to a chemical in a non-gaseous state deposited on a surface uses a light source (especially a laser) to induce release of an electron from the surface or from a second chemical optionally also deposited on the surface.

DETAILED DESCRIPTION - The method involves: (i) exposing the surface to light having an energy lower than the work function of the surface to activate an electron of the surface which is then transferred to the chemical or (ii) exposing the surface or the optional second chemical to light to release an electron from the second chemical.

An INDEPENDENT CLAIM is also included for detecting an analyte using laser desorption **mass spectrometry** using the method in which the chemical is the analyte.

USE - The method is useful for detecting analytes by laser desorption **mass spectrometry** with improved sensitivity and resolution e.g. biomolecules such as nucleic acids or proteins, drugs or drug candidates. It can also be used to detect analytes (e.g. nucleic acids labeled with polyfluoro-containing groups) not previously detectable by this technique. The method may also be useful in other procedures which utilize a chemical acquiring an extra electron e.g. in photolithographic techniques, to create reactivity sites on surfaces for immobilization of substances, to achieve welding or binding.

ADVANTAGE - The method can be used with ordinary **mass spectrometry** equipment to produce sharper and/or more intense signals from analytes and to enable detection of a wider analyte range than previous laser desorption **mass spectrometry** techniques.
Dwg.0/9

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=> fil hcapl
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FILE COVERS 1907 - 10 May 2002  VOL 136 ISS 19
FILE LAST UPDATED: 8 May 2002  (20020508/ED)
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text search

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 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

=> d que l39; d que l50; d que l52; d que l58

L35 (     23564)SEA FILE=HCAPLUS ABB=ON  (PROTEINS/CW OR PEPTIDES/CW)(L)ANT/RL

L36 (     31530)SEA FILE=HCAPLUS ABB=ON  MASS SPECTROMETRY/CW
L37 (       946)SEA FILE=HCAPLUS ABB=ON  L36(L)(CHEM? IONIZATION)
L38 (       569)SEA FILE=HCAPLUS ABB=ON  L36(L)(ATM? PRESSURE)
L39           4 SEA FILE=HCAPLUS ABB=ON  L35 AND L37 AND L38



L40       31593 SEA FILE=HCAPLUS ABB=ON  MASS SPECTROMETRY/CW
L41        3066 SEA FILE=HCAPLUS ABB=ON  L40(L)(LASER DESORPTION OR MATRIX
                ASSIS?)
L42        3497 SEA FILE=HCAPLUS ABB=ON  L40(L)(ELECTROSPRAY IONIZATION)
L43       21792 SEA FILE=HCAPLUS ABB=ON  PROTEIN#/CW(L)ANT/RL
L44        4156 SEA FILE=HCAPLUS ABB=ON  PEPTIDE#/CW(L)ANT/RL
L45      254381 SEA FILE=HCAPLUS ABB=ON  ?ISOTOP?
L49       80803 SEA FILE=HCAPLUS ABB=ON  PROTEIN DEGRADATION+NT/CT OR PROTEOLY?

L50           3 SEA FILE=HCAPLUS ABB=ON  (L43 OR L44)(L)L45 AND (L41 OR L42)
                AND L49
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- Role ANT = analyte

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L40       31593 SEA FILE=HCAPLUS ABB=ON  MASS SPECTROMETRY/CW
L43       21792 SEA FILE=HCAPLUS ABB=ON  PROTEIN#/CW(L)ANT/RL
L44        4156 SEA FILE=HCAPLUS ABB=ON  PEPTIDE#/CW(L)ANT/RL
L51          24 SEA FILE=HCAPLUS ABB=ON  SIGNATURE#(2A)PEPTIDE#
L52           4 SEA FILE=HCAPLUS ABB=ON  (L43 OR L44) AND L40 AND L51



L40       31593 SEA FILE=HCAPLUS ABB=ON  MASS SPECTROMETRY/CW
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L41        3066 SEA FILE=HCAPLUS ABB=ON  L40(L)(LASER DESORPTION OR MATRIX
                ASSIS?)
L42        3497 SEA FILE=HCAPLUS ABB=ON  L40(L)(ELECTROSPRAY IONIZATION)
L43       21792 SEA FILE=HCAPLUS ABB=ON  PROTEIN#/CW(L)ANT/RL
L44        4156 SEA FILE=HCAPLUS ABB=ON  PEPTIDE#/CW(L)ANT/RL
L45      254381 SEA FILE=HCAPLUS ABB=ON  ?ISOTOP?
L53      524513 SEA FILE=HCAPLUS ABB=ON  COVALENT? OR LABEL? OR TAG#### OR
                ACYLAT?
L57       74417 SEA FILE=HCAPLUS ABB=ON  QUANTITATIVE/TI
L58           6 SEA FILE=HCAPLUS ABB=ON  L45(5A)L53 AND (L43 OR L44) AND (L41
                OR L42) AND L57


=> s (139 or 150 or 152 or 158) not 14

L161         12 (L39 OR L50 OR L52 OR L58) NOT L4

=> fil wpids

FILE 'WPIDS' ENTERED AT 12:58:01 ON 10 MAY 2002
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FILE LAST UPDATED: 08 MAY 2002              <20020508/UP>
MOST RECENT DERWENT UPDATE            200229   <200229/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> The BATCH option for structure searches has been
    enabled in WPINDEX/WPIDS and WPIX  >>>

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY >>>

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX TOOLS OF THE
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=> d que 166; d que 170;d que 173; d que 177

L59        6505 SEA FILE=WPIDS ABB=ON  MASS SPECTR?
L65           3 SEA FILE=WPIDS ABB=ON  SIGNATURE#(2A)PEPTIDE#
L66           2 SEA FILE=WPIDS ABB=ON  L65 AND L59



L59        6505 SEA FILE=WPIDS ABB=ON  MASS SPECTR?
L63         221 SEA FILE=WPIDS ABB=ON  L59(L)(ATMOS? PRESS?)
L64          87 SEA FILE=WPIDS ABB=ON  L59(L)(CHEMICAL IONI?)
L67        9168 SEA FILE=WPIDS ABB=ON  ?ISOTOP?
L68       95101 SEA FILE=WPIDS ABB=ON  PROTEIN#
L69       51655 SEA FILE=WPIDS ABB=ON  ?PEPTIDE?
L70           2 SEA FILE=WPIDS ABB=ON  L63 AND L64 AND (L68 OR L69) AND L67



L59        6505 SEA FILE=WPIDS ABB=ON  MASS SPECTR?
L60         172 SEA FILE=WPIDS ABB=ON  L59(L)MATRIX ASSIS?
L61         151 SEA FILE=WPIDS ABB=ON  L59(L)DESORPTION IONI?
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previously printed in author search

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L62          71 SEA FILE=WPIDS ABB=ON  L59(L)(ELECTROSPRAY OR ELECTRO SPRAY)(W)
                IONI?
L63         221 SEA FILE=WPIDS ABB=ON  L59(L)(ATMOS? PRESS?)
L64          87 SEA FILE=WPIDS ABB=ON  L59(L)(CHEMICAL IONI?)
L67        9168 SEA FILE=WPIDS ABB=ON  ?ISOTOP?
L68       95101 SEA FILE=WPIDS ABB=ON  PROTEIN#
L69       51655 SEA FILE=WPIDS ABB=ON  ?PEPTIDE?
L72      125008 SEA FILE=WPIDS ABB=ON  COMPLEX
L73           3 SEA FILE=WPIDS ABB=ON  ((L60 OR L61 OR L62 OR L63 OR L64)) AND
                L67 AND L68 AND L69 AND L72



L59        6505 SEA FILE=WPIDS ABB=ON  MASS SPECTR?
L60         172 SEA FILE=WPIDS ABB=ON  L59(L)MATRIX ASSIS?
L61         151 SEA FILE=WPIDS ABB=ON  L59(L)DESORPTION IONI?
L62          71 SEA FILE=WPIDS ABB=ON  L59(L)(ELECTROSPRAY OR ELECTRO SPRAY)(W)
                IONI?
L63         221 SEA FILE=WPIDS ABB=ON  L59(L)(ATMOS? PRESS?)
L64          87 SEA FILE=WPIDS ABB=ON  L59(L)(CHEMICAL IONI?)
L67        9168 SEA FILE=WPIDS ABB=ON  ?ISOTOP?
L68       95101 SEA FILE=WPIDS ABB=ON  PROTEIN#
L69       51655 SEA FILE=WPIDS ABB=ON  ?PEPTIDE?
L74      121073 SEA FILE=WPIDS ABB=ON  DEGRAD? OR PROTEOLY? OR CLEAV? OR
                FRAGMENT?
L75       84550 SEA FILE=WPIDS ABB=ON  COVALENT? OR LABEL? OR TAG#### OR
                ACYLAT?
L77           8 SEA FILE=WPIDS ABB=ON  L67 AND L75 AND L74 AND (L60 OR L61 OR
                L62 OR L63 OR L64) AND (L68 OR L69)


=> s (166 or 170 or 173 or 177) not 1156

L162        10 (L66 OR L70 OR L73 OR L77) NOT L156

=> fil medl

FILE 'MEDLINE' ENTERED AT 12:58:05 ON 10 MAY 2002

 FILE LAST UPDATED: 9 MAY 2002 (20020509/UP). FILE COVERS 1958 TO DATE.

 On April 22, 2001, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE now contains IN-PROCESS records.  See HELP CONTENT for details.

 MEDLINE is now updated 4 times per week.  A new current-awareness alert
 frequency (EVERYUPDATE) is available.  See HELP UPDATE for more information.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2001 vocabulary.  Enter HELP THESAURUS for details.

 The OLDMEDLINE file segment now contains data from 1958 through 1965.
 Enter HELP CONTENT for details.

 Left, right, and simultaneous left and right truncation are available in the
 Basic Index.  See HELP SFIELDS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
 SUBSTANCE IDENTIFICATION.

=> d que 189;d que 193; s (189 or 193) not 1157

L80       50306 SEA FILE=MEDLINE ABB=ON  SPECTRUM ANALYSIS, MASS+NT/CT
```

previously printed

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L81        9790 SEA FILE=MEDLINE ABB=ON  ISOTOPE LABELING/CT
L82      260298 SEA FILE=MEDLINE ABB=ON  ISOTOPES+NT/CT
L83      111811 SEA FILE=MEDLINE ABB=ON  PROTEINS/CT
L84      124255 SEA FILE=MEDLINE ABB=ON  PEPTIDES/CT OR PEPTIDE FRAGMENTS/CT
L86       32038 SEA FILE=MEDLINE ABB=ON  L83(L)(AN OR CH)/CT
L87       42352 SEA FILE=MEDLINE ABB=ON  L84(L)(AN OR CH)/CT
L89           5 SEA FILE=MEDLINE ABB=ON  L86/MAJ AND L87/MAJ AND L80 AND (L81
                OR L82)
```

> subheadings AN-analysis CH-chemistry

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L80       50306 SEA FILE=MEDLINE ABB=ON  SPECTRUM ANALYSIS, MASS+NT/CT
L90          24 SEA FILE=MEDLINE ABB=ON  SIGNATURE#(2A)?PEPTIDE?
L92         936 SEA FILE=MEDLINE ABB=ON  PROTEOME/CT
L93           4 SEA FILE=MEDLINE ABB=ON  L80 AND L90 NOT L92

L163          9 (L89 OR L93) NOT L15
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previously printed

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=> fil embase

FILE 'EMBASE' ENTERED AT 12:58:07 ON 10 MAY 2002
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 FILE COVERS 1974 TO 8 May 2002 (20020508/ED)

 EMBASE has been reloaded.  Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que l104;d que l111; d que l120

L99        58543 SEA FILE=EMBASE ABB=ON  MASS SPECTROMETRY+NT/CT
L100       43227 SEA FILE=EMBASE ABB=ON  PROTEIN ANALYSIS/CT
L101      412681 SEA FILE=EMBASE ABB=ON  ISOTOPE+NT/CT OR ISOTOPE LABELING+NT/CT

L102          24 SEA FILE=EMBASE ABB=ON  SIGNATURE#(2A)?PEPTIDE?
L104           6 SEA FILE=EMBASE ABB=ON  L102 AND L99 AND (L100 OR L101)


L99        58543 SEA FILE=EMBASE ABB=ON  MASS SPECTROMETRY+NT/CT
L100       43227 SEA FILE=EMBASE ABB=ON  PROTEIN ANALYSIS/CT
L101      412681 SEA FILE=EMBASE ABB=ON  ISOTOPE+NT/CT OR ISOTOPE LABELING+NT/CT

L105       17678 SEA FILE=EMBASE ABB=ON  L100/MAJ
L106          38 SEA FILE=EMBASE ABB=ON  L105 AND L99 AND L101
L107       62012 SEA FILE=EMBASE ABB=ON  PROTEIN/CT
L108       16157 SEA FILE=EMBASE ABB=ON  PEPTIDE/CT
L111           3 SEA FILE=EMBASE ABB=ON  L106 AND L107 AND L108


L99        58543 SEA FILE=EMBASE ABB=ON  MASS SPECTROMETRY+NT/CT
L100       43227 SEA FILE=EMBASE ABB=ON  PROTEIN ANALYSIS/CT
L101      412681 SEA FILE=EMBASE ABB=ON  ISOTOPE+NT/CT OR ISOTOPE LABELING+NT/CT

L114       14448 SEA FILE=EMBASE ABB=ON  PROTEIN DETERMINATION/CT
L118        8395 SEA FILE=EMBASE ABB=ON  CHEMICAL MODIFICATION/CT
L120           3 SEA FILE=EMBASE ABB=ON  (L114 OR L100) AND L99 AND L101 AND
                L118
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```
=> s (l104 or l111 or l120) not l158

L164          9 (L104 OR L111 OR L120) NOT L158

=> fil jic biosis biotechno anabstr

FILE 'JICST-EPLUS' ENTERED AT 12:58:09 ON 10 MAY 2002
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=> d que l135; d que l139; d que l149

L124    2182509 SEA PROTEIN#
L125     485562 SEA PEPTIDE#
L127     140112 SEA MASS SPECTR?
L128     190757 SEA ISOTOP? OR RADIOISOTOP?
L133       2131 SEA L127(L) ATMOS? PRESS?
L134       5503 SEA L127(L) CHEMICAL IONI?
L135          4 SEA L133 AND L134 AND L128 AND (L124 OR L125)



L126         30 SEA SIGNATURE#(2A) PEPTIDE#
L127     140112 SEA MASS SPECTR?
L130       5541 SEA L127(L) MATRIX ASSIS?
L131       5386 SEA L127(L) DESORPTION IONI?
L132       5604 SEA L127(L)(ELECTRO SPRAY OR ELECTROSPRAY)(W) IONI?
L133       2131 SEA L127(L) ATMOS? PRESS?
L134       5503 SEA L127(L) CHEMICAL IONI?
L139          5 SEA L126 AND (L130 OR L131 OR L132 OR L133 OR L134)



L124    2182509 SEA PROTEIN#
L125     485562 SEA PEPTIDE#
L127     140112 SEA MASS SPECTR?
L128     190757 SEA ISOTOP? OR RADIOISOTOP?
L130       5541 SEA L127(L) MATRIX ASSIS?
L131       5386 SEA L127(L) DESORPTION IONI?
L132       5604 SEA L127(L)(ELECTRO SPRAY OR ELECTROSPRAY)(W) IONI?
L133       2131 SEA L127(L) ATMOS? PRESS?
L134       5503 SEA L127(L) CHEMICAL IONI?
L141     549075 SEA LABEL? OR TAG#### OR COVALENT? OR ACYLAT?
L142      13842 SEA L128(8A) L141
L143     693193 SEA PROTEOLY? OR CLEAV? OR FRAGMENT? OR DEGRAD?
L144         25 SEA L142 AND (L130 OR L131 OR L132 OR L133 OR L134) AND L143
                AND (L124 OR L125)
L147     393933 SEA QUANTITAT?
L149          3 SEA L144 AND L147

=> s (l135 or l139 or l149) not l159
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previously printed

L165 7 (L135 OR L139 OR L149) NOT L159

=> dup rem l163,l161,l165,l164,l162
FILE 'MEDLINE' ENTERED AT 13:00:01 ON 10 MAY 2002

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FILE 'ANABSTR' ENTERED AT 13:00:01 ON 10 MAY 2002

FILE 'EMBASE' ENTERED AT 13:00:01 ON 10 MAY 2002

FILE 'WPIDS' ENTERED AT 13:00:01 ON 10 MAY 2002

PROCESSING COMPLETED FOR L163
PROCESSING COMPLETED FOR L161
PROCESSING COMPLETED FOR L165
PROCESSING COMPLETED FOR L164
PROCESSING COMPLETED FOR L162
L166 40 DUP REM L163 L161 L165 L164 L162 (7 DUPLICATES REMOVED)
ANSWERS '1-9' FROM FILE MEDLINE
ANSWERS '10-19' FROM FILE HCAPLUS
ANSWER '20' FROM FILE BIOSIS
ANSWERS '21-24' FROM FILE BIOTECHNO
ANSWER '25' FROM FILE ANABSTR
ANSWERS '26-30' FROM FILE EMBASE
ANSWERS '31-40' FROM FILE WPIDS

=> d ibib ab 1-40; fil hom

L166 ANSWER 1 OF 40 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002088110 MEDLINE
DOCUMENT NUMBER: 21591313 PubMed ID: 11816564
TITLE: **Phosphopeptide** derivatization **signatures** to identify serine and threonine phosphorylated peptides by mass spectrometry.
AUTHOR: Molloy M P; Andrews P C
CORPORATE SOURCE: Department of Biological Chemistry, University of Michigan Medical School, Ann Arbor 48109-0606, USA.
CONTRACT NUMBER: RO1 CA77078-01 (NCI)
RO1HG01709-01 (NHGRI)
SOURCE: ANALYTICAL CHEMISTRY, (2001 Nov 15) 73 (22) 5387-94.
Journal code: 0370536. ISSN: 0003-2700.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020131
Last Updated on STN: 20020320
Entered Medline: 20020319
AB The development of rapid, global methods for monitoring states of protein phosphorylation would provide greater insight for understanding many

fundamental biological processes. Current best practices use mass spectrometry (MS) to profile digests of purified proteins for evidence of phosphorylation. However, this approach is beset by inherent difficulties in both identifying phosphopeptides from within a complex mixture containing many other unmodified peptides and ionizing phosphopeptides in positive-ion MS. We have modified an approach that uses barium hydroxide to rapidly eliminate the phosphoryl group of serine and threonine modified amino acids, creating dehydroamino acids that are susceptible to nucleophilic derivatization. By derivatizing a protein digest with a mixture of two different alkanethiols, phosphopeptide-specific derivatives were readily distinguished by MS due to their characteristic ion-pair signature. The resulting tagged ion pairs accommodate simple and rapid screening for phosphopeptides in a protein digest, obviating the use of isotopically labeled samples for qualitative phosphopeptide detection. MALDI-MS is used in a first pass manner to detect derivatized phosphopeptides, while the remaining sample is available for tandem MS to reveal the site of derivatization and, thus, phosphorylation. We demonstrated the technique by identifying phosphopeptides from beta-casein and ovalbumin. The approach was further used to examine in vitro phosphorylation of recombinant human HSP22 by protein kinase C, revealing phosphorylation of Thr-63.

L166 ANSWER 2 OF 40 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001558360 MEDLINE
DOCUMENT NUMBER: 21490997 PubMed ID: 11604532
TITLE: Identification of disulfide-linked peptides by isotope profiles produced by peptic digestion of proteins in 50% (18)O water.
AUTHOR: Wallis T P; Pitt J J; Gorman J J
CORPORATE SOURCE: Biomolecular Research Institute, Parkville VIC 3052, Australia.
SOURCE: PROTEIN SCIENCE, (2001 Nov) 10 (11) 2251-71.
Journal code: 9211750. ISSN: 0961-8368.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20011018
Last Updated on STN: 20020313
Entered Medline: 20020312

AB Determination of the disulfide-bond arrangement of a protein by characterization of disulfide-linked peptides in proteolytic digests may be complicated by resistance of the protein to specific proteases, disulfide interchange, and/or production of extremely complex mixtures by less specific proteolysis. In this study, mass spectrometry has been used to show that incorporation of (18)O into peptides during peptic digestion of disulfide-linked proteins in 50% (18)O water resulted in isotope patterns and increases in average masses that facilitated identification and characterization of disulfide-linked peptides even in complex mixtures, without the need for reference digests in 100% (16)O water. This is exemplified by analysis of peptic digests of model proteins lysozyme and ribonuclease A (RNaseA) by matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF) and electrospray ionization (ESI) mass spectrometry (MS). Distinct isotope profiles were evident when two peptide chains were linked by disulfide bonds, provided one of the chains did not contain the C terminus of the protein. This latter class of peptide, and single-chain peptides containing an intrachain disulfide bond, could be identified and characterized by mass shifts produced by reduction. Reduction also served to confirm other assignments. Isotope profiling of peptic digests showed that disulfide-linked peptides were often enriched in the high molecular weight fractions produced by size exclusion chromatography (SEC) of the digests. Applicability of these procedures to

analysis of a more complex disulfide-bond arrangement was shown with the hemagglutinin/neuraminidase of Newcastle disease virus.

L166 ANSWER 3 OF 40 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2000185162 MEDLINE
DOCUMENT NUMBER: 20185162 PubMed ID: 10722087
TITLE: **Signature-peptide** approach to detecting proteins in complex mixtures.
AUTHOR: Geng M; Ji J; Regnier F E
CORPORATE SOURCE: Department of Chemistry, Purdue University, West Lafayette, IN 47907, USA.
CONTRACT NUMBER: 25431
SOURCE: JOURNAL OF CHROMATOGRAPHY. A, (2000 Feb 18) 870 (1-2) 295-313.
Journal code: BXJ; 9318488.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000427
Last Updated on STN: 20000427
Entered Medline: 20000418

AB The objective of the work presented in this paper was to test the concept that tryptic peptides may be used as analytical surrogates of the protein from which they were derived. Proteins in complex mixtures were digested with trypsin and classes of peptide fragments selected by affinity chromatography, lectin columns were used in this case. Affinity selected peptide mixtures were directly transferred to a high-resolution reversed-phase chromatography column and further resolved into fractions that were collected and subjected to matrix-assisted laser desorption ionization (MALDI) mass spectrometry. The presence of specific proteins was determined by identification of **signature peptides** in the mass spectra. Data are also presented that suggest proteins may be quantified as their **signature peptides** by using isotopically labeled internal standards. Isotope ratios of peptides were determined by MALDI mass spectrometry and used to determine the concentration of a peptide relative to that of the labeled internal standard. Peptides in tryptic digests were labeled by acetylation with acetyl N-hydroxysuccinimide while internal standard peptides were labeled with the trideuteroacetylated analogue. Advantages of this approach are that (i) it is easier to separate peptides than proteins, (ii) native structure of the protein does not have to be maintained during the analysis, (iii) structural variants do not interfere and (iv) putative proteins suggested from DNA databases can be recognized by using a **signature peptide** probe.

L166 ANSWER 4 OF 40 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 1998410768 MEDLINE
DOCUMENT NUMBER: 98410768 PubMed ID: 9740052
TITLE: Identification of yeast proteins from two-dimensional gels: working out spot cross-contamination.
AUTHOR: Parker K C; Garrels J I; Hines W; Butler E M; McKee A H; Patterson D; Martin S
CORPORATE SOURCE: PerSeptive Biosystems, Framingham, MA, USA.. kenparker@pbio.com
SOURCE: ELECTROPHORESIS, (1998 Aug) 19 (11) 1920-32.
Journal code: ELE; 8204476. ISSN: 0173-0835.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901

ENTRY DATE: Entered STN: 19990128
Last Updated on STN: 19990128
Entered Medline: 19990114

AB With the complete sequence of the yeast genome now available, efforts by many laboratories are underway to identify each of the spots on two-dimensional (2-D) gels corresponding to the most abundant yeast proteins. The high mass accuracy now attainable using matrix assisted laser desorption/ionization (MALDI)-mass spectrometry equipped with delayed extraction simplifies the process of identification, such that many spots can be unambiguously identified in a short period of time merely by using peptide mass fingerprinting and generally available database matching programs. Although it is not always possible to match spots between gels run by different laboratories, proteins generally yield the same abundant proteolytic fragments when tryptic digestions are performed. Databases containing these **signature peptides** not only simplify the task of reidentifying proteins from different gels, but also make it possible to identify small amounts of cross-contaminating proteins from different spots, as well as common extraneous contaminants such as human keratins. In this paper, we present data on the identification of > 20 previously unreported yeast proteins from 2-D gels. Some novel proteins were identified from randomly analyzed spots. Focusing on 14 spots in a narrow-pH-range gel, we demonstrate how organizing peak-table data and peptide match-list data into databases enables the identification of a larger percentage of the peaks.

L166 ANSWER 5 OF 40 MEDLINE
ACCESSION NUMBER: 2002122351 MEDLINE
DOCUMENT NUMBER: 21846427 PubMed ID: 11857767
TITLE: Automated deconvolution and deisotoping of electrospray mass spectra.
AUTHOR: Wehofsky Marco; Hoffmann Ralf
CORPORATE SOURCE: Biologisch-Medizinisches Forschungszentrum (BMFZ), Heinrich-Heine-Universitat, D-40255 Dusseldorf, Germany.
SOURCE: JOURNAL OF MASS SPECTROMETRY, (2002 Feb) 37 (2) 223-9.
Journal code: 9504818. ISSN: 1076-5174.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020222
Last Updated on STN: 20020322
Entered Medline: 20020321

AB Electrospray ionization (ESI) of peptides and proteins produces a series of multiply charged ions with a mass/charge (m/z) ratio between 500 and 2000. The resulting mass spectra are crowded by these multiple charge values for each molecular mass and an isotopic cluster for each nominal m/z value. Here, we report a new algorithm simultaneously to deconvolute and deisotope ESI mass spectra from complex peptide samples based on their mass-dependent isotopic mean pattern. All signals corresponding to one peptide in the sample were reduced to one singly charged monoisotopic peak, thereby significantly reducing the number of signals, increasing the signal intensity and improving the signal-to-noise ratio. The mass list produced could be used directly for database searching. The developed algorithm also simplified interpretation of fragment ion spectra of multiply charged parent ions.

L166 ANSWER 6 OF 40 MEDLINE
ACCESSION NUMBER: 2001465614 MEDLINE
DOCUMENT NUMBER: 21401622 PubMed ID: 11510843
TITLE: Inverse 18O labeling mass spectrometry for the rapid identification of marker/target proteins.

AUTHOR: Wang Y K; Ma Z; Quinn D F; Fu E W
CORPORATE SOURCE: Core Technologies Area, Discovery Research, Novartis Pharmaceuticals Corporation, Summit, New Jersey 07901, USA.. karen.wang@pharma.novartis.com
SOURCE: ANALYTICAL CHEMISTRY, (2001 Aug 1) 73 (15) 3742-50. Journal code: 0370536. ISSN: 0003-2700.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20010821
Last Updated on STN: 20020122
Entered Medline: 20011205

AB Systematic analysis of proteins is essential in understanding human diseases and their clinical treatments. To achieve the rapid and unambiguous identification of marker or target proteins, a new procedure termed "inverse labeling" is proposed. With this procedure, to evaluate protein expression of a diseased or a drug-treated sample in comparison with a control sample, two converse labeling experiments are performed in parallel. The perturbed sample (by disease or by drug treatment) is labeled in one experiment, whereas the control is labeled in the second experiment. When mixed and analyzed with its unlabeled counterpart for differential comparison using mass spectrometry, a characteristic inverse labeling pattern of mass shift will be observed between the two parallel analyses for proteins that are differentially expressed. In this study, protein labeling is achieved through 18O incorporation into peptides by proteolysis performed in [18O]water. Once the peptides are identified with the characteristic inverse labeling pattern of 18O/16O ion intensity shift, MS data of peptide fingerprints or peptide sequence information can be used to search a protein database for protein identification. The methodology has been applied successfully to two model systems in this study. It permits quick focus on the signals of differentially expressed proteins. It eliminates the detection ambiguities caused by the dynamic range of detection on proteins of extreme changes in expression. It enables the detection of protein modifications responding to perturbation. This strategy can also be extended to other protein-labeling methods, such as chemical or metabolic labeling, to realize the same benefits.

L166 ANSWER 7 OF 40 MEDLINE
ACCESSION NUMBER: 2001428116 MEDLINE
DOCUMENT NUMBER: 21368467 PubMed ID: 11476230
TITLE: Selective, sensitive, and rapid phosphopeptide identification in enzymatic digests using ESI-FTICR-MS with infrared multiphoton dissociation.
AUTHOR: Flora J W; Muddiman D C
CORPORATE SOURCE: Department of Chemistry, Virginia Commonwealth University, Richmond 23284, USA.
CONTRACT NUMBER: R01HG02159 (NHGRI)
SOURCE: ANALYTICAL CHEMISTRY, (2001 Jul 15) 73 (14) 3305-11. Journal code: 4NR; 0370536. ISSN: 0003-2700.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010903
Last Updated on STN: 20010903
Entered Medline: 20010830

AB Rapid screening for phosphopeptides within complex proteolytic digests involving electrospray ionization Fourier transform ion cyclotron resonance mass spectrometry (ESI-FTICR-MS) in the negative ion mode with infrared multiphoton dissociation (IRMPD) accompanied by improved

[redacted]

phosphopeptide sensitivity and selectivity is demonstrated with the tryptic digests of the naturally phosphorylated proteins bovine alpha- and beta-casein. All peptides in a complex proteolytic digest can be examined simultaneously for phosphorylation with a 4-s IR laser pulse at 7-11 W where **phosphopeptide signature** ions form upon irradiation, as the low energy of activation phosphate moiety cleavage transpires without the dissociation of the unphsophorylated peptide population. The tyrosine phosphorylated peptide HGLDN-pY-R, its nonphosphorylated analogue HGLDNYR, the kinase domain of insulin receptor unphosphorylated TRDIYETDYYRK, monophosphorylated TRDIYED-pY-YRK, and triphosphorylated TRDI-pY-ETD-pY-pY-RK were also used as model peptides in this research. The sensitivity and selectivity of phosphopeptides is shown to greatly improve when the volatile base piperidine is used to adjust the pH of th

L166 ANSWER 8 OF 40 MEDLINE
ACCESSION NUMBER: 2001674499 MEDLINE
DOCUMENT NUMBER: 21577412 PubMed ID: 11720389
TITLE: Automatic analysis of hydrogen/deuterium exchange mass spectra of peptides and proteins using calculations of isotopic distributions.
AUTHOR: Palmblad M; Buijs J; Hakansson P
CORPORATE SOURCE: Division of Ion Physics, Angstrom Laboratory, Uppsala University, Sweden.. magnus.palmblad@angstrom.uu.se
SOURCE: JOURNAL OF THE AMERICAN SOCIETY FOR MASS SPECTROMETRY, (2001 Nov) 12 (11) 1153-62.
Journal code: 9010412. ISSN: 1044-0305.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011127
Last Updated on STN: 20020124
Entered Medline: 20020102

AB High mass-resolving power has been shown to be useful for studying the conformational dynamics of proteins by hydrogen/deuterium (H/D) exchange. A computer algorithm was developed that automatically identifies peptides and their extent of deuterium incorporation from H/D exchange mass spectra of enzymatic digests or fragment ions produced by collisionally induced dissociation (CID) or electron capture dissociation (ECD). The computer algorithm compares measured and calculated isotopic distributions and uses a fast calculation of isotopic distributions using the fast Fourier transform (FFT). The algorithm facilitates rapid and automated analysis of H/D exchange mass spectra suitable for high-throughput approaches to the study of peptide and protein structures. The algorithm also makes the identification independent on comparisons with undeuterated control samples. The applicability of the algorithm was demonstrated on simulated isotopic distributions as well as on experimental data, such as Fourier transform ion cyclotron resonance (FTICR) mass spectra of myoglobin peptic digests, and CID and ECD spectra of substance P.

L166 ANSWER 9 OF 40 MEDLINE
ACCESSION NUMBER: 2000424908 MEDLINE
DOCUMENT NUMBER: 20378724 PubMed ID: 10918372
TITLE: Quantitation of peptides and proteins by matrix-assisted laser desorption/ionization mass spectrometry using (18)O-labeled internal standards.
AUTHOR: Mirgorodskaya O A; Kozmin Y P; Titov M I; Korner R; Sonksen C P; Roepstorff P
CORPORATE SOURCE: Institute of Cytology, Russian Academy of Sciences, 4 Tikhoretsky pr, St. Petersburg, 194064 Russia.. oamir@link.cytspb.rssi.ru

SOURCE: RAPID COMMUNICATIONS IN MASS SPECTROMETRY, (2000) 14 (14) 1226-32.
Journal code: A9Q; 8802365. ISSN: 0951-4198.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000922
Last Updated on STN: 20000922
Entered Medline: 20000912

AB A method for quantitating proteins and peptides in the low picomole and sub-picomole range has been developed using matrix-assisted laser desorption/ionization mass spectrometry (MALDI-MS) with internal (18)O-labeled standards. A simple procedure is proposed to produce such internal standards for the tested sample by enzymatic hydrolysis of the same sample (with known concentration) in (18)O-water. A mathematical algorithm was developed which uses the isotopic patterns of the substance, the internal standard, and the substance/internal standard mixture for accurate quantitation of the substance. A great advantages of the proposed method is the absence of molecular weight limitation for the protein quantitation and the possibility of quantitation without previous fractionation of proteins and peptides. Using this strategy, the peptide angiotensinogen and two proteins, RNase and its protein inhibitor, were quantified by MALDI-time-of-flight (TOF) mass spectrometry.

L166 ANSWER 10 OF 40 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
ACCESSION NUMBER: 2001:79420 HCAPLUS
DOCUMENT NUMBER: 134:219186
TITLE: **Quantitative** proteomic analysis using a MALDI quadrupole time-of-flight mass spectrometer
AUTHOR(S): Griffin, Timothy J.; Gygi, Steven P.; Rist, Beate; Aebersold, Ruedi; Loboda, Alexander; Jilkine, Alexandra; Ens, Werner; Standing, Kenneth G.
CORPORATE SOURCE: Department of Molecular Biotechnology, University of Washington, Seattle, WA, 98195-7730, USA
SOURCE: Analytical Chemistry (2001), 73(5), 978-986
CODEN: ANCHAM; ISSN: 0003-2700
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We describe an approach to the quant. anal. of complex protein mixts. using a MALDI quadrupole time-of-flight (MALDI QqTOF) mass spectrometer and **isotope** coded affinity **tag** reagents (Gygi, S. P.; et al. Nat. Biotechnol. 1999, 17, 994-9.). Proteins in mixts. are first **labeled** on cysteinyl residues using an **isotope** coded affinity **tag** reagent, the proteins are enzymically digested, and the labeled peptides are purified using a multidimensional sepn. procedure, with the last step being the elution of the labeled peptides from a microcapillary reversed-phase liq. chromatog. column directly onto a MALDI sample target. After addn. of matrix, the sample spots are analyzed using a MALDI QqTOF mass spectrometer, by first obtaining a mass spectrum of the peptides in each sample spot in order to quantify the ratio of abundance of pairs of **isotopically tagged** peptides, followed by tandem mass spectrometric anal. to ascertain the sequence of selected peptides for protein identification. The effectiveness of this approach is demonstrated in the quantification and identification of peptides from a control mixt. of proteins of known relative concns. and also in the comparative anal. of protein expression in Saccharomyces cerevisiae grown on two different carbon sources.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L166 ANSWER 11 OF 40 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 5
ACCESSION NUMBER: 1999:558165 HCAPLUS
DOCUMENT NUMBER: 131:348704
TITLE: Protein Cross-Links: Universal Isolation and Characterization by Isotopic Derivatization and Electrospray Ionization Mass Spectrometry
AUTHOR(S): Chen, Xiaohui; Chen, Yong Hong; Anderson, Vernon E.
CORPORATE SOURCE: Department of Biochemistry, School of Medicine, Case Western Reserve University, Cleveland, OH, 44106-4935, USA
SOURCE: Analytical Biochemistry (1999), 273(2), 192-203
CODEN: ANBCA2; ISSN: 0003-2697
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A general method of unequivocally identifying and obtaining sequence information on cross-linked peptides derived by **proteolytic** digestion of cross-linked proteins has been developed. The method is based on isotopic labeling of .alpha.-amino groups with 2,4-dinitrofluorobenzene (DNFB) coupled with electrospray ionization mass spectrometry. Proteins contg. covalent cross-link(s) are reductively methylated to convert lysine residues to di-Me lysine. The methylated protein is partially hydrolyzed and the liberated .alpha.-amino termini are derivatized with an equimolar mixt. of DNFB and [2H3]DNFB. Dinitrophenyl (DNP)-labeled peptides may be fractionated into mono- and bis-DNP pools by chromatog. on Ph media. The bis-DNP peptides are further sepd. by reverse-phase HPLC and analyzed by electrospray ionization mass spectrometry. The mol. ions of cross-linked peptides are unambiguously identified as 1:2:1 triplets in the mass spectrum resulting from the binomial distribution of isotopic label in the bis-DNP deriv. Sequence information can be elucidated from the unique product ion patterns which are generated from in-source fragmentation at an elevated cone voltage. Anal. of the disulfide cross-linked peptide (VT[Ccedil]G)2 was undertaken as a proof of concept and the generality of the method was demonstrated by isolating and sequencing the isopeptide bond of polyubiquitin. (c) 1999 Academic Press.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L166 ANSWER 12 OF 40 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:737615 HCAPLUS
TITLE: The **isotope**-coded affinity **tag** reagent method for **quantitative** proteomics
AUTHOR(S): Aerbersold, Ruedi; Gygi, Steven P.; Griffin, Timothy J.; Han, David. K. M.; Yelle, Michael J.
CORPORATE SOURCE: Univ. of Washington, Seattle, WA, USA
SOURCE: American Genomic/Proteomic Technology (2001), 1(1), 22, 24, 26-27
CODEN: AGTMC7; ISSN: 1537-0003
PUBLISHER: International Scientific Communications, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **Isotope**-coded Affinity **Tag** (ICAT) reagent method, first described by Gygi et al. and recently commercialized by Applied Biosystems (Foster City, CA) enables the concurrent quantification and identification of proteins in complex mixts. It is based on a new class of chem. reagents termed **isotope**-coded affinity **tags** used in conjunction with tandem MS and multidimensional liq. chromatog. The method addresses several limitations of two-dimensional PAGE (2D-PAGE)-based proteomic expts. It has been shown to successfully identify and quantify both low-abundance and membrane proteins, classes that are typically difficult to analyze by 2D-PAGe. Automation is enabled

by using a tandem MS instrument (API QSTARTM system with oMaldiTM and electrospray ion sources, from Applied Biosystems and MDS Sciex [Toronto, Ontario, Canada]) for performing expression-dependent protein identification.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L166 ANSWER 13 OF 40 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:145059 HCAPLUS
DOCUMENT NUMBER: 132:191408
TITLE: Rapid **quantitative** analysis of proteins or protein function in complex mixtures using affinity labeling reagents and mass spectrometry
INVENTOR(S): Aebersold, Rudolf Hans; Gelb, Michael H.; Gygi, Steven P.; Scott, C. Ronald; Turecek, Frantisek; Gerber, Scott A.; Rist, Beate
PATENT ASSIGNEE(S): University of Washington, USA
SOURCE: PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000011208	A1	20000302	WO 1999-US19415	19990825
W: AU, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9956913	A1	20000314	AU 1999-56913	19990825
EP 1105517	A1	20010613	EP 1999-943915	19990825
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1998-97788P P 19980825
US 1998-99113P P 19980903
WO 1999-US19415 W 19990825
OTHER SOURCE(S): MARPAT 132:191408

AB Anal. reagents and mass spectrometry-based methods using these reagents for the rapid, and quant. anal. of proteins or protein function in mixts. of proteins are disclosed. The methods employ affinity labeled protein reactive reagents having three portions: an affinity label (A) covalently linked to a protein reactive group (PRG) through a linker group (L). The linker may be differentially **isotopically labeled**, e.g., by substitution of one or more atoms in the linker with a stable isotope thereof. These reagents allow for the selective isolation of peptide fragments or the products of reaction with a given protein (e.g., products of enzymic reaction) from complex mixts. The isolated peptide fragments or reaction products are characteristic of the presence of a protein or the presence of a protein function in those mixts. Isolated peptides or reaction products are characterized by mass spectrometric (MS) techniques. The reagents also provide for differential **isotopic labeling** of the isolated peptides or reaction products which facilitates quant. detn. by mass spectrometry of the relative amt. of proteins in different samples. The methods of this invention can be used for qual. and quant. anal. of global protein expression profiles in cells and tissues, to screen for and identify proteins whose expression level in cells, tissue or biol. fluids is affected by a stimulus or by a change in condition or cell state of the cell, tissue or organism from which the sample originated. A conjugate of N-methylglycylbiotinamide acid and the Michael addn. product of 4,7,10-trioxa-1,13-tridecanediamine and p-acrylamidophenyl-.beta.-D-galactopyranoside was prepd. for detecting .beta.-D-galactosidase deficiency and GM1-gangliosidosis.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L166 ANSWER 14 OF 40 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:107471 HCAPLUS
DOCUMENT NUMBER: 132:290640
TITLE: Site-Specific Mass Tagging with Stable Isotopes in Proteins for Accurate and Efficient Protein Identification
AUTHOR(S): Chen, Xian; Smith, Lloyd M.; Bradbury, E. Morton
CORPORATE SOURCE: Chemical Science Technology Division Bioscience Division, Los Alamos National Laboratory, Los Alamos, NM, 87544, USA
SOURCE: Analytical Chemistry (2000), 72(6), 1134-1143
CODEN: ANCHAM; ISSN: 0003-2700
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Proteolytic** peptide mass mapping as measured by mass spectrometry provides a major approach for the identification of proteins. A protein is usually identified by the best match between the measured and calcd. m/z values of the **proteolytic** peptides. A unique identification is, however, heavily dependent upon the mass accuracy and sequence coverage of the fragment ions generated by peptide ionization. Without ultrahigh instrumental accuracy, it is possible to increase the specificity of the assignments of particular **proteolytic** peptides by the incorporation of selected amino acid residue(s) enriched with stable isotope(s) into the protein sequence. Here we report this novel method of generating residue-specific mass-tagged **proteolytic** peptides for accurate and efficient protein identification. Selected amino acids are labeled with 13C/15N/2H and incorporated into proteins in a sequence-specific manner during cell culturing. Each of these labeled amino acids carries a defined mass change encoded in its monoisotopic distribution pattern. Through their characteristic patterns, the peptides with mass tags can then be readily distinguished from other peptides in mass spectra. This method of identifying unique proteins can also be extended to protein complexes and will significantly increase data search specificity, efficiency, and accuracy for protein identifications.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L166 ANSWER 15 OF 40 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:735650 HCAPLUS
DOCUMENT NUMBER: 134:53327
TITLE: **Quantitative** determination of peptides and proteins by MALDI MS
AUTHOR(S): Mirgorodskaya, O. A.; Koz'min, Yu. P.; Titov, M. I.; Savel'eva, N. V.; Korner, R.; Sonksen, C.; Miroshnikov, A. I.; Roepstorff, P.
CORPORATE SOURCE: Institute of Cytology, Russian Academy of Sciences, St. Petersburg, 194064, Russia
SOURCE: Russian Journal of Bioorganic Chemistry (Translation of Bioorganicheskaya Khimiya) (2000), 26(9), 593-602
CODEN: RJBCET; ISSN: 1068-1620
PUBLISHER: MAIK Nauka/Interperiodica
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A modified method of isotope diln. was applied to the quant. detn. of peptides and proteins by MALDI MS at sub-picomolar level. The essence of the method consists in the quant. anal. of the enzymic hydrolysis products rather than the starting compds. This allows the measurements to be performed at a higher resoln. and makes the method independent of the mol.

mass of oligopeptides and proteins examd. Fragments obtained by hydrolysis of the same oligopeptide or protein in a known concn. by the same enzyme and **labeled** with the stable 18O **isotope** are used as internal stds. The label is introduced by carrying out the hydrolysis in H218O, and the oligopeptide concn. is calcd. from the **isotope** distribution between the **labeled** and unlabeled hydrolysis products in the mass spectrum. This method was tested in the detn. of concns. of the angiotensinogen (1-14) fragment (oligopeptide), extracellular RNase from Bacillus amyloliquefaciens (protein) and its protein inhibitor, barstar M. Usefulness of this method in kinetic studies was also demonstrated.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L166 ANSWER 16 OF 40 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:171061 HCAPLUS
DOCUMENT NUMBER: 133:190138
TITLE: Assessing normal levels of phytoestrogens in a general population survey
AUTHOR(S): Rogers, Helen Schurz; Blount, Ben; Needham, Larry
CORPORATE SOURCE: Health Studies Branch, Centers for Disease Control and Prevention, Atlanta, GA, USA
SOURCE: Journal of Medicinal Food (1999), 2(3-4), 215-217
CODEN: JMFOFJ; ISSN: 1096-620X
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Detns. of total environmental estrogen exposure depend on knowledge of the actual background levels of suspected endocrine disruptors and phytoestrogens in the general population. The authors have developed a method that measures these chems. in human urine using atm.-pressure chem. ionization with liq. chromatog.-tandem mass spectrometry. The authors demonstrate this method with presentation of a time-course study of concns. before and after consumption of a soy-based drink.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L166 ANSWER 17 OF 40 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:130928 HCAPLUS
DOCUMENT NUMBER: 128:254873
TITLE: HPLC-mass spectrometry analysis of isoflavones
AUTHOR(S): Barnes, Stephen; Coward, Lori; Kirk, Marion; Sfakianos, Jeff
CORPORATE SOURCE: Departments of Biochemistry & Molecular Genetics, University of Alabama at Birmingham, Birmingham, AL, 35294, USA
SOURCE: Proceedings of the Society for Experimental Biology and Medicine (1998), 217(3), 254-262
CODEN: PSEBAA; ISSN: 0037-9727
PUBLISHER: Blackwell Science, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The current interest in the role of dietary isoflavonoids, particularly the soy isoflavone genistein, in lowering the risk of several chronic diseases, has led to the need for rapid, sensitive and precise assays for isoflavones and their metabolites in food matrixes and in various physiol. fluids and tissues. HPLC has the advantage over GC-based methods in that all the conjugated and unconjugated isoflavonoids and their metabolites can be sepd. and analyzed without the need for derivatization. An important advance in mass spectrometry has been the introduction of effective interfaces between the HPLC and the mass spectrometer, namely the electrospray ionization (ESI) and the heated nebulizer-atm. pressure chem. ionization (HN-APCI) interfaces. Because of the isoflavonoid

[redacted]

concns. in fluids such as bile or urine, preliminary extn., so essential for GC-MS and many other anal. methods, is not necessary. This immediately overcomes the thorny issue of finding an effective solid-phase extn. procedure. Using reversed-phase HPLC-ESI-MS, it is possible to obtain a mass/intensity map of all isoflavonoid metabolites in a single 20 min anal. Anal. of isoflavonoid conjugates in serum/plasma samples requires initial extn., but the conjugates can be measured intact either by capillary reversed-phase HPLC-ESI-MS or on regular reversed-phase columns by HPLC-HN-APCI-MS. In both cases, specificity is obtained by causing the parent isoflavonoid mol. ions to undergo collision-induced dissocn. to form specific daughter ions in a triple quadrupole MS instrument. When it is only necessary to measure the total isoflavonoids and their metabolites in blood, hydrolysis can be performed directly in serum/plasma samples and isoflavonoids recovered by ether or Et acetate solvent extn. The isoflavone aglucones can be analyzed by HPLC-MS under isocratic solvent conditions, thereby drastically shortening anal. time and opening up prospects for automation. Therefore, HPLC-MS is a technique that is broadly applicable to the major issues in phytoestrogen research.

L166 ANSWER 18 OF 40 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:117631 HCAPLUS
DOCUMENT NUMBER: 128:228214
TITLE: A novel method for the identification of peptides in complex mixtures by tandem mass spectrometry with atmospheric pressure chemical ionization
AUTHOR(S): Beaumont, Claire; Grimble, George K.; Welham, Kevin J.
CORPORATE SOURCE: AgrEvo UK Limited, Saffron Walden, Essex, CB10 1XL, UK
SOURCE: Portland Press Proc. (1998), 11(Peptides in Mammalian Protein Metabolism), 167-176
CODEN: POPPEF; ISSN: 0966-4068
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This paper describes the initial development of an efficient, semiautomated liq. chromatog.-tandem mass spectrometric method using atmospheric pressure chem. ionization. This method allows the rapid identification of dipeptides in complex mixts. (in particular, protein hydrolyzates).

L166 ANSWER 19 OF 40 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:415275 HCAPLUS
DOCUMENT NUMBER: 122:182457
TITLE: **Quantitative** bioanalysis using matrix-assisted laser desorption/ionization mass spectrometry
AUTHOR(S): Jespersen, S.; Niessen, W. M. A.; Tjaden, U. R.; van der Greef, J.
CORPORATE SOURCE: Leiden/Amsterdam Cent. Drug Res., Leiden Univ., Leiden, 2300 RA, Neth.
SOURCE: J. Mass Spectrom. (1995), 30(2), 357-64
CODEN: JMSPFJ; ISSN: 1076-5174
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The application of matrix-assisted laser desorption/ionization mass spectrometry (MALDI-MS) for quant. anal. was investigated with the use of internal stds. Three peptides/proteins in the mass range 1000-12,000 were tested and the effect of various internal stds. was evaluated. Horse cytochrome c was used as an internal std. for bovine cytochrome c, melittin for renin and an undecapeptide B analog was employed as an internal std. for the decapeptide A. A linear response was found between the measured peak height ratio and the applied amt. of analyte when an appropriate internal std. was used. The quant. abilities of MALDI-MS were

finally applied to the detn. of the drug amperozide in plasma. The biol. samples were prepd. for anal. using liq.-liq. extn. prior to MALDI-MS. A linear calibration graph was obtained using the 13C4 stable **isotopically labeled** amperozide as an internal std.

L166 ANSWER 20 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:79117 BIOSIS
DOCUMENT NUMBER: PREV200000079117
TITLE: Application of liquid chromatography **atmospheric pressure chemical ionization** tandem **mass spectrometry** in the quantitative analysis of glyburide (glibenclamide) in human plasma.
AUTHOR(S): Ramos, L.; Bakhtiar, R. (1); Tse, F.
CORPORATE SOURCE: (1) Novartis Pharm. Corporation, 59 Route 10, Bldg 405, Room 229, East Hanover, NJ USA
SOURCE: Rapid Communications in Mass Spectrometry, (1999) Vol. 13, No. 24, pp. 2439-2443.
ISSN: 0951-4198.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Glyburide (glibenclamide) is widely prescribed in the treatment of Type II diabetes. A validated liquid chromatography **atmospheric pressure chemical ionization** tandem **mass spectrometry** (LC/APCI-MS/MS) method for the determination of glyburide is reported. The method uses a stable **isotope** labeled glyburide as the internal standard. Subsequent to acetonitrile **protein** precipitation, the supernatant was directly (unfiltered) injected onto the LC column (retention time apprx3 min) for analysis. A lower limit of quantification (LLOQ) of 1.01 ng/mL was attained for the human plasma assay. The method was fast, specific, and exhibited excellent ruggedness. It was successfully applied to the analysis of clinical samples from patients dosed with glyburide.

L166 ANSWER 21 OF 40 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 2002:34251281 BIOTECHNO
TITLE: Noladin ether, a putative novel endocannabinoid: Inactivation mechanisms and a sensitive method for its quantification in rat tissues
AUTHOR: Fezza F.; Bisogno T.; Minassi A.; Appendino G.; Mechoulam R.; Di Marzo V.
CORPORATE SOURCE: V. Di Marzo, Endocannabinoid Research Group, Istituto di Chimica Biomolecolare, Consiglio Nazionale delle Ricerche, Via Campi Flegrei 34, 80078 Pozzuoli (Naples), Italy.
E-mail: vdimarzo@icmib.na.cnr.it
SOURCE: FEBS Letters, (27 FEB 2002), 513/2-3 (294-298), 17 reference(s)
CODEN: FEBLAL ISSN: 0014-5793
PUBLISHER ITEM IDENT.: S0014579302023414
DOCUMENT TYPE: Journal; Article
COUNTRY: Netherlands
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The occurrence of the novel proposed endocannabinoid, noladin ether (2-arachidonyl glyceryl ether, 2-AGE) in various rat organs and brain regions, and its inactivation by intact C6 glioma cells, were studied. 2-AGE was measured by **isotope** dilution liquid chromatography-**atmospheric pressure chemical ionization-mass spectrometry**, with a detection limit of 100 fmol. A compound with the same mass and chromatographic/chemical properties as 2-AGE was found in whole brain,

with the highest amounts in the thalamus and hippocampus. Synthetic [.sup.3H]2-AGE was inactivated by intact rat C6 glioma cells by a time- and temperature-dependent process consisting of cellular uptake and partial incorporation into phospholipids. Further data suggested that 2-AGE is taken up by cells via the anandamide/2-arachidonoyl glycerol (2-AG) membrane transporter(s), and biosynthesized in a different way as compared to 2-AG. .COPYRGT. 2002 Published by Elsevier Science B.V. on behalf the Federation of European Biochemical Societies.

L166 ANSWER 22 OF 40 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 2002:34183423 BIOTECHNO
TITLE: **Quantitative** proteomics strategy involving the selection of **peptides** containing both cysteine and histidine from tryptic digests of cell lysates
AUTHOR: Wang S.; Zhang X.; Regnier F.E.
CORPORATE SOURCE: F.E. Regnier, Department of Chemistry, 3164A Brown Building, Purdue University, West Lafayette, IN 47907-1393, United States.
E-mail: fregnier@purdue.edu
SOURCE: Journal of Chromatography A, (08 MAR 2002), 949/1-2 (153-162), 34 reference(s)
CODEN: JCRAEY ISSN: 0021-9673
PUBLISHER ITEM IDENT.: S0021967301015096
DOCUMENT TYPE: Journal; Article
COUNTRY: Netherlands
LANGUAGE: English
SUMMARY LANGUAGE: English
AB This paper describes a procedure for **quantitative** proteomics that selects **peptides** containing both cysteine and histidine residues from tryptic digests of cell lysates. Cysteine-containing **peptides** were selected first by covalent chromatography using thiol disulfide exchange. Following the release of cysteine-containing **peptides** from the covalent chromatography column with reductive **cleavage**, histidine-containing **peptides** were captured by passage through an immobilized metal affinity chromatography column loaded with copper. Quantification was achieved in a four-step process involving (i) differential **labeling** of control and experimental samples with **isotopically** differing forms of succinic anhydride, (ii) mixing the two globally labeled samples, (iii) fractionating the labeled **peptides** by reversed-phase liquid chromatography, and (iv) determining the isotope ratio in individual **peptides** by mass spectrometry. The results of these studies indicate that by selecting **peptides** containing both cysteine and histidine, the complexity of **protein** digests could be substantially reduced. Up-regulated **proteins** from plasmid bearing Escherichia coli that had been induced with isopropyl .beta.-thiogalacto-pyranoside were identified and quantified by the global internal standard technology (GIST) described above. Database searches were greatly simplified because the number of possible **peptide** candidates was reduced more than 95%. .COPYRGT. 2002 Elsevier Science B.V. All rights reserved.

L166 ANSWER 23 OF 40 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 2000:30482510 BIOTECHNO
TITLE: Detection and quantification of neurotensin in human brain tissue by **matrix-assisted** laser **desorption/ionization** time-of- flight **mass spectrometry**
AUTHOR: Gobom J.; Kraeuter K.-O.; Persson R.; Steen H.; Roepstorff P.; Ekman R.
CORPORATE SOURCE: R. Ekman, Institute of Clinical Neuroscience, SU/Moelndal Hospital, Goteborg University, S-43180

Searched by Barb O'Bryen, STIC 308-4291

Moelndal, Sweden.
E-mail: rolf.ekman@neuro.gu.se
SOURCE: Analytical Chemistry, (15 JUL 2000), 72/14 (3320-3326)
CODEN: ANCHAM ISSN: 0003-2700
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A method was developed for **mass spectrometric** detection of neurotensin (NT)-like immunoreactivity and quantification of NT in human brain tissue. The method is based on immunoprecipitation followed by analysis using **matrix-assisted** laser **desorption/ionization** time-of-flight **mass spectrometry** (MALDI- TOF-MS). The identity of the major component of the immunoprecipitates as neurotensin was confirmed by **fragment** ion analysis on an **electrospray ionization** quadrupole time-of-flight instrument. MALDI-TOF-MS quantification of NT was achieved using stable-**isotope-labeled** NT as the internal standard, yielding an error of less than 5%. The method allowed detection of low- femtomole amounts of NT, starting from low-milligram amounts of lyophilized brain tissue. In addition to NT, several other **peptides** were detected in the purified samples, most of which, according to their molecular masses, corresponded to **fragments** of NT. The method is demonstrated with quantification of NT from human hypothalamus tissue, and a comparison is made with results obtained from competitive radioimmunoassay.

L166 ANSWER 24 OF 40 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 1998:28097416 BIOTECHNO
TITLE: Clinical analysis of sampatrilat, a combined renal endopeptidase and angiotensin-converting enzyme inhibitor. II: Assay in the plasma and urine of human volunteers by dissociation enhanced lanthanide fluorescence immunoassay (DELFIA)
AUTHOR: Venn R.F.; Barnard G.; Kaye B.; Macrae P.V.; Saunders K.C.
CORPORATE SOURCE: R.F. Venn, Department of Drug Metabolism, Pfizer Central Research, Sandwich CT13 9NJ, United Kingdom.
SOURCE: Journal of Pharmaceutical and Biomedical Analysis, (1998), 16/5 (883-892), 4 reference(s)
CODEN: JPBADA ISSN: 0731-7085
PUBLISHER ITEM IDENT.: S0731708597001271
DOCUMENT TYPE: Journal; Article
COUNTRY: Netherlands
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Sampatrilat is a dual inhibitor of angiotensin converting enzyme (ACE) and neutral endopeptidase (NEP) under development for the treatment of hypertension and congestive heart failure. In order to support the early clinical development (with oral administration and an expected low bioavailability), a sensitive and selective assay was required. An HPLC-**atmospheric-pressure chemical ionisation mass-spectrometric** (HPLC-APCI-MS-MS) assay had been validated, but due to its low throughput an alternative method was sought. As the molecule is **peptide** -like and not metabolised, we believed the immunoassay approach was appropriate. Thus we developed an immunoassay for the compound using time-resolved fluorescence as an end-point (DELFIA.RTM.) with lower limits of quantification of 0.2 ng m.sup.-.sup.1 for the plasma assay and 5 ng ml.sup.-.sup.1 for the assay in urine. This assay is a 96-well plate based competitive immunoassay; the end-point is the determination of a (non-radioactive) europium label by time-resolved fluorimetry.

Sampatrilat is labelled with chelated europium via isothiocyanate chemistry. The advantage of this assay is its extremely high throughput, allowing rapid analysis of many thousands of samples. The DELFIA method was successfully cross-validated with the HPLC-APCI-MS-MS method.

L166 ANSWER 25 OF 40 ANABSTR COPYRIGHT 2002 RSC

AB Serum (200 .mu.l) was mixed with 2 .mu.g labelled 1,3-.cents.15N2-13C]theophylline (LTH; internal standard). **Proteins** were removed by ultrafiltration or by addition of 50 .mu.l TCA (50 mg/ml H2O) followed by centrifugation. The deproteinized solution was directly injected on to a 7 .mu.m Nucleosil C18 column (25 cm .times. 4.6 mm i.d.). Elution (1.5 ml/min) was with 0.05% acetic acid/methanol (1:1). MS spectra were recorded on the SSQ 7000 Finnigan system with an electrospray ionization/atmospheric-pressure CI interface (operating conditions given). Vaporizer and capillary were held at 400 and 150.degree.C, respectively. Spectra were recorded at 1800 V. Calibration graphs were linear from 0.5-30 .mu.g/ml theophylline (TH); RSD was <2% (n = 2) with LTH/TH (1:1). Within- and between- run precisions were 0.88-1.5% and 0.9-1.5%, respectively. The detection limit was 10 ng/ml at a signal-to-noise ratio of 3:1. Results are compared with those obtained using GC-**isotope** dilution MS, HPLC and FPIA; there was good comparability (results tabulated).

L166 ANSWER 26 OF 40 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2002136040 EMBASE

TITLE: Residue-specific mass signatures for the efficient detection of protein modifications by mass spectrometry.

AUTHOR: Zhu H.; Hunter T.C.; Pan S.; Yau P.M.; Bradbury E.M.; Chen X.

CORPORATE SOURCE: X. Chen, Chemistry Division, BN-2, Los Alamos National Laboratory, Los Alamos, NM 87544, United States. chen_xian@lanl.gov

SOURCE: Analytical Chemistry, (1 Apr 2002) 74/7 (1687-1694). Refs: 25
ISSN: 0003-2700 CODEN: ANCHAM

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Currently available mass spectrometric (MS) techniques lack specificity in identifying protein modifications because molecular mass is the only parameter used to characterize these changes. Consequently, the suspected modified peptides are subjected to tandem MS/MS sequencing that may demand more time and sample. We report the use of stable isotope-enriched amino acids as residue-specific "mass signatures" for the rapid and sensitive detection of protein modifications directly from the peptide mass map (PMM) without enrichment of the modified **peptides**. These mass **signatures** are easily recognized through their characteristic spectral patterns and provide fingerprints for peptides containing the same content of specific amino acid residue(s) in a PMM. Without the need for tandem MS/MS sequencing, a peptide and its modified form(s) can readily be identified through their identical fingerprints, regardless of the nature of modifications. In this report, we demonstrate this strategy for the detection of methionine oxidation and protein phosphorylation. More interestingly, the phosphorylation of a histone protein, H2A.X, obtained from human skin fibroblast cells, was effectively identified in response to low-dose radiation. In general, this strategy of residue-specific mass tagging should be applicable to other posttranslational modifications.

L166 ANSWER 27 OF 40 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002136039 EMBASE
TITLE: Using stable-isotope-labeled proteins for hydrogen exchange studies in complex mixtures.
AUTHOR: Engen J.R.; Bradbury E.M.; Chen X.
CORPORATE SOURCE: X. Chen, Chemistry Division, BN-2, Los Alamos National Laboratory, Los Alamos, NM 87545, United States. chen_xian@lanl.gov
SOURCE: Analytical Chemistry, (1 Apr 2002) 74/7 (1680-1686). Refs: 33
ISSN: 0003-2700 CODEN: ANCHAM
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The use of mass spectrometry to measure hydrogen exchange rates for individual proteins in complex mixtures is described. Incorporation of stable-isotope-labeled (SIL) amino acids into a protein of interest during overexpression in bacteria produced distinctive isotope patterns in mass spectra of peptic peptides from the labeled protein. The isotope pattern was used as a **signature** for **peptides** originating from the SIL protein. In addition, stable-isotope labeling simplified identification of the peptic peptides by providing partial amino acid composition information. Despite the complex isotope patterns associated with SIL peptides, hydrogen exchange rates could still be measured for peptides from SIL protein and were found to be the same as exchange rates for unlabeled protein. Hydrogen exchange in a single protein of interest was measured in a complex mixture of proteins, a bacterial cell lysate. This methodology, which includes easy recognition of peptic peptides from the protein(s) of interest during hydrogen exchange studies in heterogeneous systems, will permit analysis of structural properties and dynamics of large protein complexes and complex protein systems.

L166 ANSWER 28 OF 40 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002125364 EMBASE
TITLE: Stable isotope labelling in vivo as an aid to protein identification in peptide mass fingerprinting.
AUTHOR: Pratt J.M.; Robertson D.H.L.; Gaskell S.J.; Riba-Garcia I.; Hubbard S.J.; Sidhu K.; Oliver S.G.; Butler P.; Hayes A.; Petty J.; Beynon R.J.
CORPORATE SOURCE: Prof. R.J. Beynon, Dept. of Veterinary Preclinical Sci., University of Liverpool, Crown Street, Liverpool L69 7ZJ, United Kingdom. r.beynon@liv.ac.uk
SOURCE: Proteomics, (2002) 2/2 (157-163). Refs: 8
ISSN: 1615-9853 CODEN: PROTC7
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Peptide mass fingerprinting (PMF) is a powerful technique for identification of proteins derived from in-gel digests by virtue of their matrix-assisted laser desorption/ionization-time of flight mass spectra. However, there are circumstances where the under-representation of peptides in the mass spectrum and the complexity of the source proteome mean that PMF is inadequate as an identification tool. In this paper, we show that identification is substantially enhanced by inclusion of composition data for a single amino acid. Labelling in vivo with a stable isotope labelled amino acid (in this paper, decadeuterated leucine)

identifies the number of such amino acids in each digest fragment, and show a considerable gain in the ability of PMF to identify the parent protein. The method is tolerant to the extent of labelling, and as suc, may be applicable to a range of single cell systems.

L166 ANSWER 29 OF 40 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001301226 EMBASE
TITLE: Synthesis of d-labeled N-alkylmaleimides and application to quantitative peptide analysis by isotope differential mass spectrometry.
AUTHOR: Niwayama S.; Kurono S.; Matsumoto H.
CORPORATE SOURCE: S. Niwayama, Department of Chemistry, Oklahoma State University, Stillwater, OK 74078-3071, United States. niwayama@biochem.okstate.edu
SOURCE: Bioorganic and Medicinal Chemistry Letters, (3 Sep 2001) 11/17 (2257-2261).
Refs: 21
ISSN: 0960-894X CODEN: BMCLE8
PUBLISHER IDENT.: S 0960-894X(01)00452-8
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB d-Labeled N-alkylmaleimides have been prepared for specific modification of the terminal SH groups of cysteine residues in proteins or peptides. These reagents are useful tools for quantitative analysis of peptides by stable isotope differential mass spectrometry. .COPYRGT. 2001 Elsevier Science Ltd. All rights reserved.

L166 ANSWER 30 OF 40 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001343233 EMBASE
TITLE: Analytical techniques: From individual proteins to whole cells.
AUTHOR: Robinson C.V.; Cowburn D.
CORPORATE SOURCE: C.V. Robinson, Oxford Centre for Molecular Sciences, South Parks Road, Oxford OX1 3QT, United Kingdom. carolr@bioch.ox.ac.uk
SOURCE: Current Opinion in Chemical Biology, (1 Oct 2001) 5/5 (565-566).
ISSN: 1367-5931 CODEN: COCBF4
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
029 Clinical Biochemistry
LANGUAGE: English

L166 ANSWER 31 OF 40 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-147802 [19] WPIDS
DOC. NO. CPI: C2002-045872
TITLE: Highly parallel analysis of polymorphisms, useful e.g. for diagnosis and prognosis of disease, by extending immobilized primers hybridized to templates.
DERWENT CLASS: B04-D16
INVENTOR(S): BERLIN, K; GUT, I G
PATENT ASSIGNEE(S): (EPIG-N) EPIGENOMICS AG
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001098527	A2	20011227	(200219)*	GE	35

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DK DM DZ
EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG
SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
DE 10029914 A1 20020103 (200219)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001098527	A2	WO 2001-DE2273	20010619
DE 10029914	A1	DE 2000-10029914	20000619

PRIORITY APPLN. INFO: DE 2000-10029914 20000619
AB WO 200198527 A UPAB: 20020321
NOVELTY - Highly parallel characterization of polymorphisms by:
(a) binding a set of probes (P) to an addressable surface;
(b) hybridizing test nucleic acid (I) to P;
(c) extending P by allele-specific reaction, depending on sequence of (I) serving as template;
(d) treating with an exonuclease (II) that **degrades** unextended, but not extended, P; and
(e) analysis of remaining allele-specific extension products.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a kit comprising at least one primer pair for amplification;
(2) a set of (P);
(3) enzyme; and
(4) buffer and instructions for performing the new method.
USE - For highly parallel characterization of polymorphisms (claimed). Especially the method is useful for (i) genotyping known polymorphisms; (ii) identifying new polymorphisms and/or (iii) detecting and visualizing cytosine methylation patterns.
Specific applications are diagnosis and/or prognosis of: side effects of drugs; cancer; central nervous system disorders; aggression/behavioral disorders; brain damage; psychotic or personality disorders; cardiovascular, gastrointestinal or respiratory diseases; injury; inflammation; infection; convalescence; disorders of development, skin, muscle, connective tissue and bone; endocrine or metabolic disorders; headache and sexual dysfunction. It can also be used to differentiate between cell types and tissues, also for studying cell differentiation.
ADVANTAGE - The highly parallel method is more efficient than current processes as regards simplicity, cost, quality and throughput, and makes possible simultaneous detection of both cytosine methylation pattern and polymorphisms.
Dwg.0/4

L166 ANSWER 32 OF 40 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-216735 [27] WPIDS
DOC. NO. NON-CPI: N2002-166189
DOC. NO. CPI: C2002-066155
TITLE: Encoding (**labeling**) several **polypeptide** samples for analysis by mass spectrometry by **cleaving** amide backbone of the **polypeptides** in each sample and mass modifying the carboxy terminus of the **fragments** obtained.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): FIGEYS, J M D; MANN, M; STEWART, I I
PATENT ASSIGNEE(S): (MDSP-N) MDS PROTEOMICS INC
COUNTRY COUNT: 95

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001094935	A2	20011213	(200227)*	EN	67

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001070941 A 20011217 (200229)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001094935	A2	WO 2001-IB1328	20010608
AU 2001070941	A	AU 2001-70941	20010608

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001070941	A	Based on	WO 200194935

PRIORITY APPLN. INFO: US 2001-293664P 20010525; US 2000-210496P 20000609

AB WO 200194935 A UPAB: 20020429

NOVELTY - Encoding (**labeling**) several **polypeptide** samples for analysis by mass spectrometry by **cleaving** amide backbone of the **polypeptides** in each sample and mass modifying the carboxy terminus of the **fragments** obtained

DETAILED DESCRIPTION - Encoding (**labeling**) (M1) several **polypeptide** samples for analysis by mass spectrometry comprises:

(a) **cleaving** the amide backbone of **polypeptides** of each individual sample to form sub-populations of **fragments** (I) having carboxy-terminal residues (CTR);

(b) mass-modifying the CTRs of (I) with one of at least two groups of different molecular weight (MWt) to produce several discrete populations of mass-modified (I) which differ in MWt by the addition of the group, where the groups differ in MWt due to inclusion of isotypes of differing MWt, where for each sample, the mass-modification produces several various discrete populations **labeled**, in a predetermined ratio of at least two groups, where the ratio of each sample is different from the next amongst **polypeptide** samples.

INDEPENDENT CLAIMS are also included for the following:

(1) producing (M2) a **peptide** sample pool (PSP) for analysis by mass spectrometry comprising forming a **peptide** digest (PDI) by hydrolyzing a **peptide** sample in the presence of a water containing a volumetric ratio of two members of an **isotope**, forming a **peptide** digest (PD2) by repeating the above method, where the volumetric ratios of PD1 and PD2 are different from each other; and pooling PD1 and PD2 to form a **peptide** sample;

(2) PSP produced by M2, which is adapted to reveal the **protein** source of each **peptide** in the pool when the pool is analyzed by mass spectrometry, comprising PD1 and PD2; and

(3) a software program for high throughput automated analysis of mass spectrometry data of **peptide** sample comprises identifying desired **peptides** in a sample with high probability based on their mass data, generating a theoretical natural **isotope** abundance distribution based on the identification of the **peptides**, subtracting the relative **isotopic** contribution by each of the

labeled states and comparing them in a relative sense to generate the 160/180 of desired ratio.

USE - M1 is useful for quantitating the abundance of a given **polypeptide** present in a sample using mass spectrometry. The method comprises carrying out M1, where the mass-modified portions obtained or combined to form a **peptide** sample and subjected to analysis by mass spectrometry to mass spectra comprising at least one signal doublet for each **fragment** where the signal doublet comprises a first signal and a second signal that shifted a known amount of units from the first signal. The method further comprises determining a signal ratio for at least a **fragment** pair by relating the difference in signal intensity or area between the first and second signal, where the abundance of the given **polypeptide** is determined from the signal ratio and the known amount of the standard sample of the given **polypeptide**, based on the principle that signal intensity is proportional to **peptide** abundance. M2 is useful for producing PSP for analysis by mass spectrometry. The method is useful for tracking the source of every desired **polypeptide**, in a PSP comprising generating PSP by M2 and identifying the source of every desired **polypeptide** utilizing the PSP. PSP is useful for identifying the source of **peptide** subjected as a PSP to analyze by mass spectrometry. The method comprises obtaining PSP by M2; subjecting the **peptide** sample to analysis by mass spectrometry to generate mass spectra comprising at least one signal doublet for each **peptide** in the sample, where the signal doublet comprises a first signal and second signal shifted a known units from the first signal, where the known units is the difference in MWt between the two **isotopes**; determining a signal ratio for a given **peptide** by relating the difference in signal intensity or area between the first signal and the second signal; correlating the signal ratio for the given **peptide** with the **isotope** ratio used to form the given **peptide**, thereby identifying the **protein** source of the given **peptide** (all claimed).

ADVANTAGE - **Peptides** are **labeled** in terms of spreads based on a probability function for a given relative composition of H2180 in a digestion mixture rather than specific ratios. This reduces the absolute capability of 180 **labeling** for use as an encryption tool for the purpose of running multiple samples in tandem to reduce analysis time.

Dwg.0/11

L166 ANSWER 33 OF 40 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-154580 [20] WPIDS
DOC. NO. NON-CPI: N2002-117574
DOC. NO. CPI: C2002-048271
TITLE: Rapid, simple analysis of **complex** chemical mixtures, e.g. from chemical or enzymatic reactions or fermentation processes, using **matrix assisted** laser **desorption-ionization** time-of-flight **mass spectrometry**.
DERWENT CLASS: B04 D16 J04 S03
INVENTOR(S): HEINZLE, E; WITTMANN, C
PATENT ASSIGNEE(S): (BADI) BASF AG
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001094910	A2	20011213	(200220)*	GE	51

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK

DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU
SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
DE 10027801 A1 20011213 (200220)
AU 2001069058 A 20011217 (200225)
DE 10044132 A1 20020314 (200226)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001094910	A2	WO 2001-EP6415	20010606
DE 10027801	A1	DE 2000-10027801	20000607
AU 2001069058	A	AU 2001-69058	20010606
DE 10044132	A1	DE 2000-10044132	20000906

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001069058	A	Based on	WO 200194910

PRIORITY APPLN. INFO: DE 2000-10044132 20000906; DE 2000-10027801 20000607

AB WO 200194910 A UPAB: 20020402
NOVELTY - A method for qualitatively or quantitatively analyzing **complex** mixtures (A) of chemical compounds involves use of MALDI-TOF (**matrix assisted** laser **desorption-ionization** time-of-flight) **mass spectrometry**.
USE - (A) are specifically mixtures obtained by chemical or enzymatic reactions or fermentation processes, comprising polymeric and/or non-polymeric compounds; and the process is manual or automatic, specifically a high throughput screening or bioflow analysis (all claimed). Typically the products of combinatorial syntheses can be screened rapidly. The analytes include e.g. **proteins**, polysaccharides or polynucleotides (as polymeric compounds) or sugars, aminoacids, di- or **tripeptides**, carboxylic acids, terpenes, steroids, carotenoids, vitamins or antibiotics (as non-polymeric compounds). (A) may also be food, pharmaceutical or environmental samples.
ADVANTAGE - MALDI-TOF **mass spectrometry** is a simple, direct and rapid analysis method for **complex** mixtures.
DESCRIPTION OF DRAWING(S) - The figure shows the spectrum of a 2.5 mM mixture of lysine, alanine, glucose and sucrose in a 2,5-dihydroxybenzoic acid matrix. (Drawing includes non-English language text).
Dwg.1a/20

L166 ANSWER 34 OF 40 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-034446 [04] WPIDS
CROSS REFERENCE: 2001-596913 [62]; 2001-602751 [62]; 2001-602752 [62]; 2001-657177 [68]; 2002-010834 [68]; 2002-010922 [68]; 2002-010923 [68]; 2002-017444 [68]; 2002-017469 [68]; 2002-017470 [68]; 2002-017471 [68]; 2002-090046 [03]; 2002-130908 [09]; 2002-130909 [09]; 2002-139900 [09]; 2002-147896 [09]; 2002-154757 [10]; 2002-154758 [10]; 2002-154759 [10]; 2002-171649 [10]
DOC. NO. CPI: C2002-009658
TITLE: New nucleic acid derived from genes associated with DNA repair, useful for diagnosis, e.g. of ataxia telangiectasia, by determination of cytosine methylation.
DERWENT CLASS: A89 B04 D16
INVENTOR(S): BERLIN, K; OLEK, A; PIEPENBROCK, C
PATENT ASSIGNEE(S): (EPIG-N) EPIGENOMICS AG
COUNTRY COUNT: 95

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001081622	A2	20011101	(200204)*	EN	25

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001078420 A 20011107 (200219)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001081622	A2	WO 2001-EP3972	20010406
AU 2001078420	A	AU 2001-78420	20010406

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001078420	A	Based on	WO 200181622

PRIORITY APPLN. INFO: DE 2000-10043826 20000901; DE 2000-10019058 20000406; DE 2000-10019173 20000407; DE 2000-10032529 20000630

AB WO 200181622 A UPAB: 20020409

NOVELTY - Nucleic acid (I) containing a sequence of at least 18 nucleotides of chemically treated DNA (II) of genes associated with DNA repair, and their complements, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a nucleic acid comprising at least 18 base pairs of the chemically pretreated DNA of genes associated with DNA repair selected from PMS2L1, PMS2L12, PMS2L2, PMS2L3, PMS2,L4, PMS2L5, PMS2L6, MGMT, MSH2, NUDT1, TDG, INPPL1, RFC4, DDIT1L, FANCB, or XRCC8;

(2) an oligomer (Ia), particularly an oligonucleotide (ON) or **peptide** nucleic acid (PNA), of at least 9 nucleotides that hybridizes with, or is identical with, (II), and its complement;

(3) set of (Ia);

(4) preparing an array of (Ia) on a carrier, for analyzing diseases associated with the methylation status of CpG dinucleotides of the specified genes or (II);

(5) the array prepared by the method of (3);

(6) DNA and/or PNA array for analyzing diseases associated with methylation status of genes, comprising at least one (I);

(7) determining genetic and/or epigenetic parameters for diagnosis and/or therapy of diseases (or predisposition to them) by analyzing cytosine methylation; and

(8) kit comprising (Ia) and a bisulfite.

USE - (I), and related oligomers, are useful for diagnosis of diseases associated with gene repair, specifically ataxia telangiectasia; aging; Bloom's, Cockayne, Nijmegen break or Werner syndromes; immunodeficiency; trichthiodystrophy; Fanconi anemia; solid tumors and cancer, particularly by determining status of cytosine methylation and/or by detecting single-nucleotide polymorphisms. Determination of individual methylation patterns may allow development of individualized therapies. Dwg.0/1

L166 ANSWER 35 OF 40 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2002-049285 [06] WPIDS
DOC. NO. CPI: C2002-013845
TITLE: Highly parallel characterization of polymorphisms, useful e.g. for genotyping, by extension reaction of primers immobilized on addressable array of nucleic acid.
DERWENT CLASS: B04 D16
INVENTOR(S): BERLIN, K; GUT, I G
PATENT ASSIGNEE(S): (EPIG-N) EPIGENOMICS AG
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001081620	A2	20011101	(200206)*	GE	33

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

DE 10021204	A1	20011108	(200206)
AU 2001065759	A	20011107	(200219)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001081620	A2	WO 2001-DE1607	20010425
DE 10021204	A1	DE 2000-10021204	20000425
AU 2001065759	A	AU 2001-65759	20010425

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001065759	A	Based on	WO 200181620

PRIORITY APPLN. INFO: DE 2000-10021204 20000425
AB WO 200181620 A UPAB: 20020128
NOVELTY - Highly parallel characterization of polymorphisms.
DETAILED DESCRIPTION - Highly parallel characterization of polymorphisms, which can be used for the simultaneous or separate detection of DNA methylations. A set of probes (I) each with at least one characteristic **label**, is fixed to an addressable surface using bonds, that can be **cleaved** later, (photo)chemically or enzymatically. Test nucleic acid (NA) is hybridized to (I) which are altered by allele-specific enzymatic reactions. A part of (I) that is not important for analysis of the reaction is removed and allele-specific products are analyzed from the **label** present to determine which alleles are present in the NA sample.
USE - The method is used for the genotyping of known polymorphisms, particularly single nucleotide polymorphisms, for identifying new polymorphisms or for detection/visualization of cytosine methylation.
ADVANTAGE - The method is more effective than known processes as regards simplicity, cost, quality and throughput.
Dwg.0/5

L166 ANSWER 36 OF 40 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-017393 [02] WPIDS
DOC. NO. NON-CPI: N2002-013934
DOC. NO. CPI: C2002-004930
TITLE: Method for **labeling proteins**, useful for identification, particularly in expression analysis,

by blocking lysine sidechains, **proteolysis** and N-terminal **labeling** of **peptide fragments**.

DERWENT CLASS: B03 B04 S03
INVENTOR(S): JAMES, P
PATENT ASSIGNEE(S): (PROT-N) PROTEOME SYSTEMS LTD
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001074842	A1	20011011	(200202)*	EN	27

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001043949 A 20011015 (200209)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001074842	A1	WO 2001-AU366	20010403
AU 2001043949	A	AU 2001-43949	20010403

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001043949	A	Based on	WO 200174842

PRIORITY APPLN. INFO: AU 2000-6643 20000403

AB WO 200174842 A UPAB: 20020109
NOVELTY - Method for **labeling** a **protein** (I) by protecting epsilon -amino groups of Lys in (I), **cleaving** to produce a mixture of **peptides** (II) and treating (II) with a **labeling** agent (III) that binds to the N-terminal amino acid.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) method for identifying and/or characterizing (I) comprising **labeling** with the new method, then detecting/measuring the amount of **label** on (II);

(2) method for comparing or determining expression of (I) in two different cells by applying method (1); and

(3) use of two or more differentially **isotopically labeled** succinylation agents for **labeling peptides** and/or **proteins**.

USE - The method is used for identifying **proteins**, e.g. for analysis of **proteins** expressed by cells in different expression states.

ADVANTAGE - The method makes possible relative **protein** quantitation in one- or two-dimensional gel separations, even when separation is only partial, and facilitates de novo sequencing and automated interpretation of mass spectra. Protection of Lys sidechains ensures specific **labeling** of the N-termini; increases the intensity of b-ions (permitting full-length sequence coverage for **peptides** of m/z over 1000) and allows differentiation between Lys and Glu. The use of different **isotopic labels** allows different **proteins** in the same gel spot to be quantified.
Dwg.0/4

L166 ANSWER 37 OF 40 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2001-541652 [60] WPIDS
DOC. NO. CPI: C2001-161708
TITLE: Determining the sequence of a polynucleotide for detection of, diagnosis of or prognosis of disease i.e. cancer and Alzheimer's disease.
DERWENT CLASS: B04 D16
INVENTOR(S): JARVIK, J W
PATENT ASSIGNEE(S): (SEQU-N) SEQUEL GENETICS INC
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001061028	A2	20010823	(200160)*	EN	64

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2001041522 A 20010827 (200176)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001061028	A2	WO 2001-US5058	20010216
AU 2001041522	A	AU 2001-41522	20010216

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001041522	A	Based on	WO 200161028

PRIORITY APPLN. INFO: US 2000-189310P 20000314; US 2000-182816P 20000216

AB WO 200161028 A UPAB: 20011018
NOVELTY - Determining, (D1), the sequence of a polynucleotide comprising providing a nucleic acid fragment, (F), having a homology of a known reference sequence, (RF), expressing at least one polypeptide, (P), from it and assessing at least one physical property of at least one P to determine the sequence of F, by comparing a property to the predicted properties of a P encoded by RF, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:
(1) genetic analysis comprising D1;
(2) assessment of a disease;
(3) assessment of a disease, condition, genotype or phenotype comprises D1 and correlating the determined sequence with the disease, condition, genotype or phenotype;
(4) diagnostic or prognostic test for a disease, condition, genotype or phenotype comprises D1;
(5) assessment of a disease, condition, genotype or phenotype;
(6) diagnosis or prognosis of a disease, condition, genotype or phenotype;
(7) a data structure useful for detecting and analyzing DNA polymorphisms;
(8) a computer storage medium;
(9) a computer implemented method to identify an F encoding P, where F is a fragment of RF. The F is of known RF.
(10) a relational data set is useful for detecting and analyzing DNA mutations and polymorphisms;

(11) a computer program for searching for the data set of (10);
(12) genetic analysis comprising;
(i) providing two or more nucleic acids samples derived from two or more heterogeneous biological samples;
(ii) expressing polypeptides from each nucleic acid sample;
(iii) subjecting P, in combination, to physical property assessment; and
(iv) comparing the results of the physical property assessment to the predicted properties encoded in at least one RF; and
(13) providing a nucleic acid molecule.
USE - The method, D1, has application for the detection of,diagnosis or prognosis of genetic disease. The diseases include Alzheimer's disease, Ataxia talangietasia, familial ademato us polyposis, hereditary breast and ovarian cancer, HNPCC, retinoblastoma, Wilm's tumor, Li-Fraumeni syndrome, endocrine neoplasia, Von Hippel-Lindau syndrome, congenital adrenal hyperpalsia, androgen receptor deficiency, tetrhydrobiopterin deficiency, X-linked agammaglobulinemia, Cystic Fibrosis, diabetes, muscular dystrophy, Factor X deficiency, mitochondrial gene deficiency and Factor VII deficiency. The loci include ATM, APC, BRCA1, BRCA2, CDK2, CDKN2, hMSH2, hMLH1, hPMS1, hPMS2, RB1, WT1, p53, MEN1, MEN2, VHL, CFTR, DMD, BMD and RP.
Dwg.0/0

L166 ANSWER 38 OF 40 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2001-049881 [06] WPIDS
DOC. NO. NON-CPI: N2001-038232
DOC. NO. CPI: C2001-013716
TITLE: Determining three dimensional structure of **polypeptide** or nucleic acid molecules, by use of an integrated technique of determining physical distance constraints and analysis of constraint information.
DERWENT CLASS: B04 S03
INVENTOR(S): DOLLINGER, G; GIBSON, B W; HEMPEL, J C; KUNTZ, I D; OSHIRO, C M; TANG, N; TAYLOR, E
PATENT ASSIGNEE(S): (REGC) UNIV CALIFORNIA
COUNTRY COUNT: 92
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000072004	A2	20001130	(200106)*	EN	80

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000052989 A 20001212 (200115)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000072004	A2	WO 2000-US14667	20000526
AU 2000052989	A	AU 2000-52989	20000526

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000052989 A	Based on	WO 200072004

PRIORITY APPLN. INFO: US 1999-135891P 19990526

Dwg.0/4

L166 ANSWER 40 OF 40 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-561495 [47] WPIDS
DOC. NO. CPI: C1999-163579
TITLE: Analyzing structure of biomolecular targets and characterizing specific binding agents by mass spectrometry, used e.g. for drug screening.
DERWENT CLASS: A96 B04 D16
INVENTOR(S): CROOKE, S T; GRIFFEY, R; HOFSTADLER, S
PATENT ASSIGNEE(S): (ISIS-N) ISIS PHARM INC
COUNTRY COUNT: 85
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9945150	A1	19990910	(199947)*	EN	119
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9929773	A	19990920	(200007)		
EP 1060270	A1	20001220	(200105)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
US 6329146	B1	20011211	(200204)		
JP 2002505443	W	20020219	(200216)		142
AU 742699	B	20020110	(200217)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9945150	A1		WO 1999-US4560	19990302
AU 9929773	A		AU 1999-29773	19990302
EP 1060270	A1		EP 1999-911036	19990302
			WO 1999-US4560	19990302
US 6329146	B1	Provisional	US 1998-76534P	19980302
		CIP of	US 1998-76206	19980512
			US 1999-260310	19990302
JP 2002505443	W		WO 1999-US4560	19990302
			JP 2000-534681	19990302
AU 742699	B		AU 1999-29773	19990302

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9929773	A	Based on	WO 9945150
EP 1060270	A1	Based on	WO 9945150
JP 2002505443	W	Based on	WO 9945150
AU 742699	B	Previous Publ.	AU 9929773
		Based on	WO 9945150

PRIORITY APPLN. INFO: US 1998-76206 19980512; US 1998-76534P 19980302; US 1999-260310 19990302

AB WO 9945150 A UPAB: 20011203
NOVELTY - Mass spectrometric methods for determining the structure of nucleic acids and relative affinities of binding agents, and for identifying binding sites and binding compounds, optionally in a combinatorial mixture.
DETAILED DESCRIPTION - To determine the three-dimensional (3D)

structure of a nucleic acid (I), a chimeric version (Ia) of (I) with at least one modified subunit at a selected position, is ionized in a mass spectrometer, at least one ion **fragmented**, and **fragmentation** data related to the 3D structure.

INDEPENDENT CLAIMS are also included for the following:

(1) identifying binding sites for a ligand (L) in a biomolecular target (T);

(2) determining relative binding affinities of a binding agent (BA) for T;

(3) identifying a compound, optionally present in a (combinatorial) mixture, that binds to a selected T;

(4) identifying binding sites in T for compounds in a combinatorial library;

(5) determining relative binding affinity for T of compounds in a combinatorial mixture;

(6) screening many T against a BA, combinatorial library of compounds, or L;

(7) determining the nature and extent of binding of L to a molecular interaction site in T;

(8) identifying chemicals that bind with high specificity and affinity to a molecular interaction site in RNA; and

(9) identifying, in a mixture of compounds, those that bind to T.

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - The methods are used to determine structures of nucleic acids, sites of ligand-target interaction, and relative affinity of ligands, particularly to screen mixtures of chemicals or combinatorial libraries for compounds having potential use as pharmaceuticals, veterinary drugs, agricultural or industrial chemicals etc.

ADVANTAGE - Many targets and/or potential binding agents may be screened simultaneously and rapidly, while providing structural information about the target and ligand at the same time. Specificity of interaction may also be assessed and problems of target mass redundancy and peak overlap can be eliminated by use of molecular weight modifying **tags**.

Dwg.0/33

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